INTRAMOLECULAR ADDITION REACTIONS OF ARYL RADICALS

A THESIS

PRESENTED FOR THE DEGREE OF

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by

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CONTENTS

SUMMARY

We have demonstrated that intramolecular cyclization reactions of aryl radicals, with ortho substituents containing C=C double bonds in the 5-6 or 6-7 position relative to the radical centre, occur with great ease.

We have also been able to confirm that the reduction of aryl iodides with tri-n-butylstannane proceeds by a radical mechanism.

From accurate product studies we were able to estimate the rate constants of these aryl radical cyclization reactions, and to establish that such intramolecular ring closure reactions occur by radical attack at that end of the terminal C=C bond which is nearer to the benzene ring.

We have also been able to estimate the rate constants of two intramolecular hydrogen-atom abstraction reactions of aryl radicals; these probably constitute the only quantitative data available for such reactions.

Furthermore by electron spin resonance investigations we have observed the spectra due to the cyclic radical intermediates of intramolecular aryl radical cyclization reactions.

STATEMENT

This thesis contains no material previously submitted for a degree or diploma in any University, and to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference is made in the text.

WILLIAM B. GARA

ACKNOWLEDGEMENTS

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PUBLICATIONS

Part of this work has been published in the following communications:-

A. L. J. Beckwith and W. B. Gara, J. Amer. Chem. Soc., 91, 5689 (1969)

A. L. J. Beckwith and W. B. Gara, J. Amer. Chem. Soc., 91, 5691 (1969)

(see at the back)

PART I

INTRODUCTION

CHAPTER 1

INTERMOLECULAR ADDITION OF FREE RADICALS TO OLEFINS

1.1. ADDITION OF ALKYL RADICALS AND RELATED SPECIES

This topic will be considered briefly in order that it may be contrasted later with analogous intramolecular reactions. In particular, the main point of interest will be the direction of addition of alkyl radicals to unsymmetrically substituted olefins.

Pioneering work by Kharasch and his school established that good yields of monomeric adducts are obtained when hydrogen bromide,[1] carbon tetrachloride,[2] chloroform[2] and various aldehydes[3] are allowed to react with olefins in the presence of radical initiators. In each case, they proposed a radical chain mechanism to account for the observed products. The suggested mechanism for this type of reaction involves initial attack by the radical at the less highly substituted end of the double bond to form an intermediate radical adduct, which is converted to a stable product by radical chain transfer with a molecule of the addend.

More recently Hey, Cadogan and their co-workers[4] found that active methylene compounds such as malonic, acetoacetic and cyanoacetic esters add to olefins in the presence of radical initiators giving monomeric adducts in good yields.

The analogous radical-initiated addition reactions of perfluoroalkyl iodides to olefins were examined in detail by Haszeldine and his group.[5] In 1957 Haszeldine and Steele[6]

reported that a mixture of the two possible adducts obtained from the radical reactions of both trifluoromethyl iodide and hydrogen bromide with trifluoroethylene was: "the first example of anything other than exclusive or predominant (> 95%) radical or atomic attack on one carbon of an unsymmetrical olefin". Their rationale for these results was that the two intermediate radical adducts, formed by attack at one or the other end of the double bond of trifluoroethylene, were of similar thermodynamic stability. On this basis neither mode of attack would predominate; however this was in contrast with observations for other olefins.[6]

The work described above documents the statement that, in general, intermolecular radical additions to C=C double bonds proceed predominantly or exclusively via the thermodynamically more stable of the two possible intermediate radical adducts. Discussions of this topic are included in a number of standard textbooks[7] concerned with radical reactions.

1.2. THE TRANSITION STATE IN FREE RADICAL ADDITION REACTIONS

Szwarc and Binks[8] proposed the schematic representation of the energy factors involved in the addition of radical R• to an unsaturated molecule as shown in Figure 1.2.I.

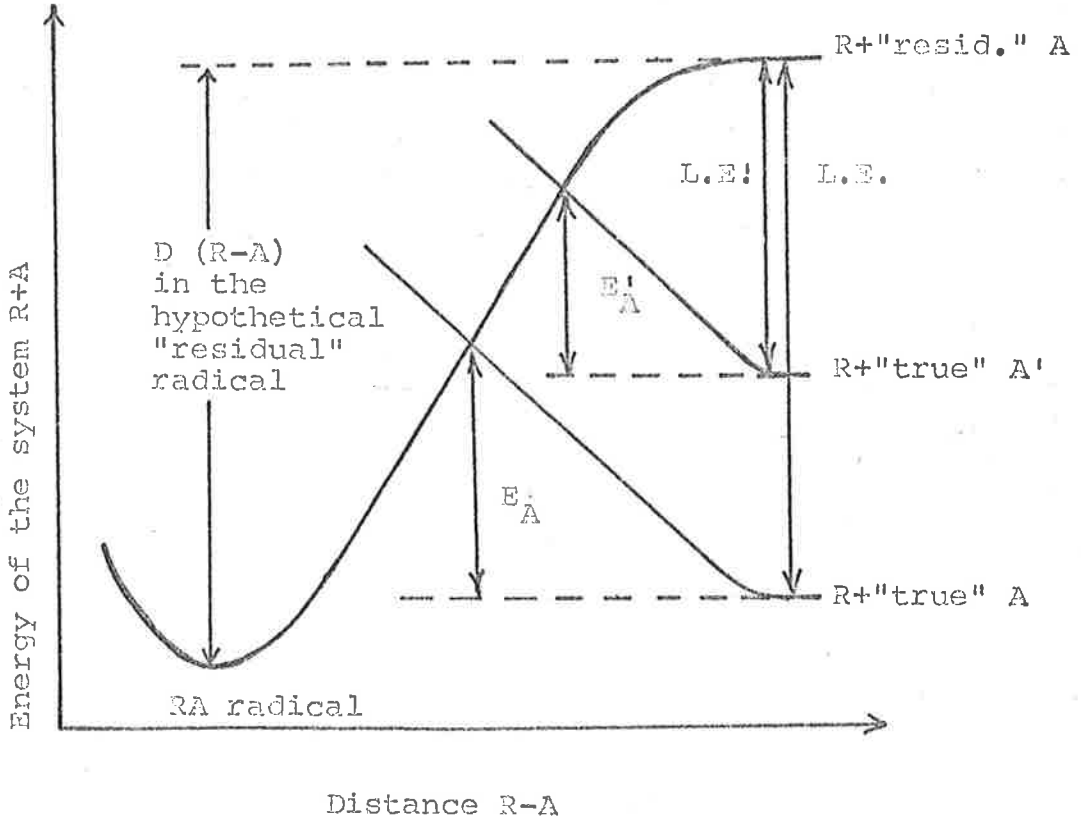


Figure 1.2.I

Their explanation of the above diagram was the following:- Molecule A is diamagnetic and all its electrons are coupled, thus none are available for the formation of the new C-C bond which would link R• to A in the radical RA•. This means

that radical R$^{\bullet}$ approaching A is repelled and the energy of the system increases as the distance between R$^{\bullet}$ and A decreases. On the other hand, the reaction may be considered as taking place between radical R$^{\bullet}$ and a "residual" molecule A in which one electron from the π-system has been localized at the carbon atom of the site of attack. By definition, the localized electron is prevented from interacting with the other electrons. This reaction process may then be represented by a Morse attraction curve in which the energy of the system decreases as the distance R-A gets smaller. The exact shape of this attraction curve is independent of the structure of A since the centre of reaction is, by definition, isolated from the rest of the molecule. Hence the C-C bond-dissociation energy in the hypothetical radical R-A "residual" is a constant, whilst D(R-A) in the "real" radical RA$^{\bullet}$ does depend on the structure of A. The latter value is given by the difference in the levels of RA$^{\bullet}$ "real" (not shown in Figure 1.2.I) and R$^{\bullet}$ + A, while the former is given by the difference in the levels of RA$^{\bullet}$ "residual" (the bottom of the Morse curve in Figure 1.2.I) and R$^{\bullet}$ + A "residual". The energy of RA$^{\bullet}$ "real" is less than the energy of RA$^{\bullet}$ "residual" because of changes in the interatomic distances in the "real" radical, whilst those in the "residual" radical are the same as in the isolated molecule A, by nature of the definition.

They suggested, furthermore, that the point of inter-

section of the repulsion and attraction curves represents the transition state in the addition reaction. This means that the atomic framework of A remains the same in the initial and in the transition state, with the exception of the configuration around the radical centre. The height of the intersection point in respect to the R°+ A level is the activation energy of the process.

It was proposed that when the reaction of a different substrate A' with the same radical R° is considered, the only change will be the relative position of the Coulombic repulsion curve with respect to the attraction curve (see Figure 1.2.I). Consequently variations in the activation energy are caused by variations in the relevant localization energies.

An illustrative example of the above proposal may be found in the work of Szwarc and his collaborators.[9,10] They examined the activation energies and the entropies of activation of the addition of trifluoromethyl radicals to a number of terminal olefins in gas[9] and liquid[10] phase. They found that 2,3-dimethyl-1,3-butadiene (A' in Figure 1.2.I) was 200 times more reactive towards trifluoromethyl radical addition than vinyl fluoride (A in Figure 1.2.I). The calculated difference in the activation energies of these two reactions was 3.4 kcal/mole; only a very small difference was observed in the respective entropies of activation. It is quite clear that

the localization energy of 2,3-dimethyl-1,3-butadiene should be much smaller than that of vinyl fluoride, since in the former the other electron, from the double bond, which is not residing at the reaction centre is stabilized by resonance; no such stabilization is available in the case of vinyl fluoride.

Szwarc[11] attempted to deduce the direction of approach of the attacking species towards the reactive site of the double bond. The A factors for the addition of methyl radicals to cis- and trans-stilbene were used as the basis of this work. They considered two extreme modes of approach, that is, either in a direction perpendicular to the nodal plane of the C=C double bond, or along the C=C axis. They suggested that approach perpendicularly to the nodal plane is hindered only in the case of the cis isomer; they reasoned that in the event of such an approach the A factor should be considerably smaller for the reaction of cis-stilbene than that for the reaction of the trans isomer. The experimentally determined A factor for the cis isomer was in fact somewhat higher than that for the trans isomer; they concluded that preferential approach should be along the C=C axis.

In a later communication Matsuoka and Szwarc[12] reported the secondary deuterium effect in the addition of methyl radicals to styrene and α,β,β-trideuterostyrene. They

calculated that a change in configuration at the reaction centre from trigonal to tetrahedral should lead to an isotope effect of 1.82. The experimentally determined value of the isotope effect was about 1.1. They concluded, therefore, that only a slight deviation occurs in the configuration of the transition state from that of the initial state. The smallness of the effect observed was taken to indicate that the incipient $C-CH_3$ bond, formed in the transition state, is comparatively long, and also that the formerly advocated concept of radical approach along the C=C axis[11] is definitely erroneous.

In a review titled:- "Stereochemistry of Free Radical Addition to Olefins", Bohm and Abell[13] favoured the view that radicals attacking a double bond approach it from a direction perpendicular to the sigma-bond of the bond in question. They stated that such a view is in agreement with the molecular orbital treatment of Greenwood.[14]

1.3. ADDITION OF ARYL RADICALS

The arylation of olefinic compounds by diazonium halides with copper salt catalysts is known as the "Meerwein reaction".

The following free-radical mechanism, which has been suggested[15] for the Meerwein reaction, is included in Rondestvedt's[16] comprehensive review on this topic:

$$ArN_2^+ + CuCl_2^- \longrightarrow Ar\text{-}N{=}N^\bullet + CuCl_2$$

$$Ar\text{-}N{=}N^\bullet \longrightarrow Ar^\bullet + N_2$$

$$Ar^\bullet + \begin{array}{|c|c|}\hline \multicolumn{2}{|c|}{} \\ \hline \multicolumn{2}{|c|}{C{=}C} \\ \hline \multicolumn{2}{|c|}{} \\ \hline \end{array} \longrightarrow Ar\text{-}\begin{array}{|c|c|}\hline \multicolumn{2}{|c|}{} \\ \hline \multicolumn{2}{|c|}{C\text{-}C^\bullet} \\ \hline \multicolumn{2}{|c|}{} \\ \hline \end{array}$$

$$Ar\text{-}\begin{array}{|c|c|}\hline \multicolumn{2}{|c|}{} \\ \hline \multicolumn{2}{|c|}{C\text{-}C^\bullet} \\ \hline \multicolumn{2}{|c|}{} \\ \hline \end{array} + CuCl_2 \longrightarrow Ar\text{-}\begin{array}{|c|c|}\hline \multicolumn{2}{|c|}{} \\ \hline \multicolumn{2}{|c|}{C\text{-}C\text{-}Cl} \\ \hline \multicolumn{2}{|c|}{} \\ \hline \end{array} + CuCl$$

These reactions are the best documented examples of the addition of aryl radicals to olefins.

Recently Werner and Ruchardt[17] presented further evidence in favour of the free-radical nature of the Meerwein reaction.

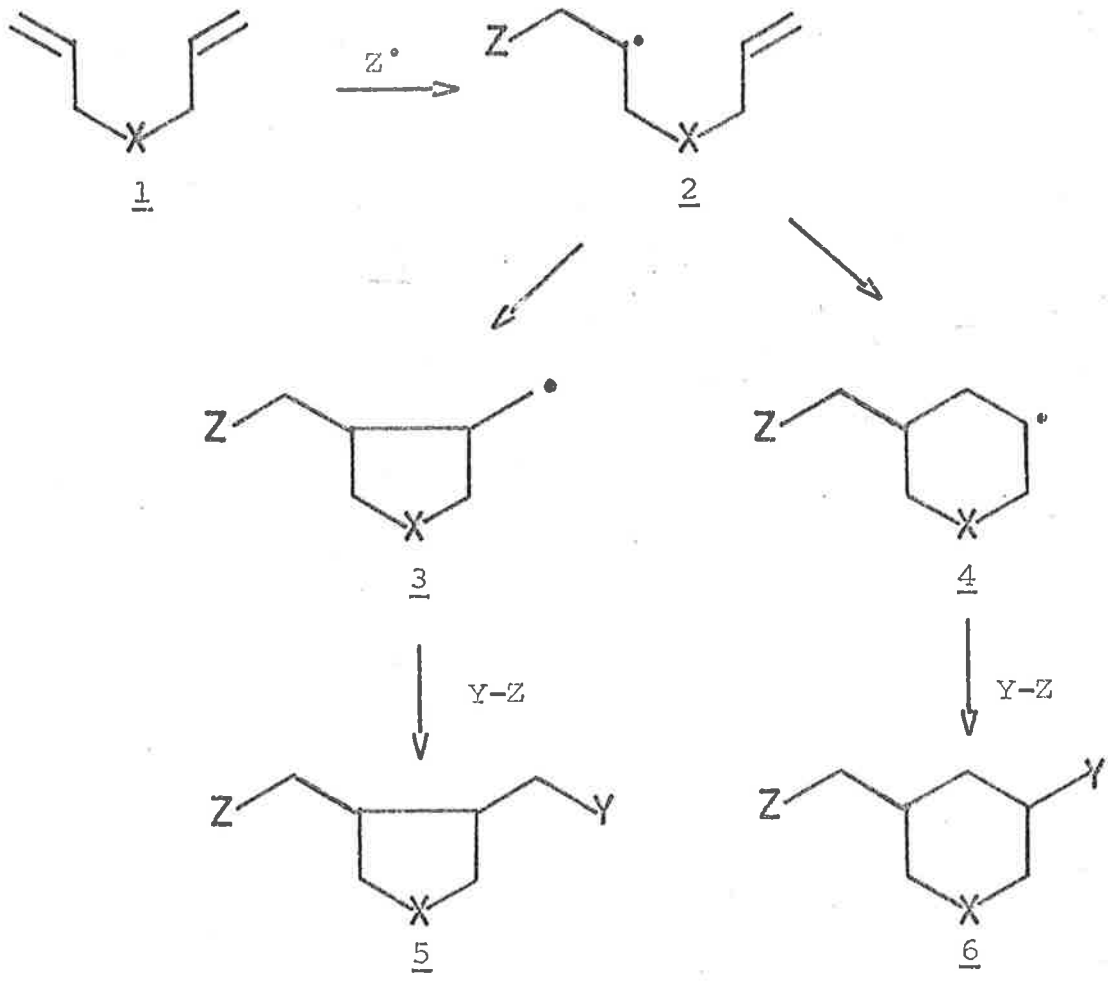
The application of electron spin resonance spectroscopic techniques to the observation of radical intermediates in these radical addition processes will be discussed later.

CHAPTER 2

INTRAMOLECULAR ADDITION OF FREE RADICALS TO OLEFINS.

2.1. CYCLIZATION OF RADICALS FORMED BY FREE RADICAL ADDITION TO TERMINAL DIENES

The course of these reactions may be represented in the abbreviated form as shown in Scheme 2.1.I, which, however does not show the 1:1 and the 2:1 uncyclized adducts that are also formed in these reactions.



Scheme 2.1.I

Radical polymerization reactions of heptadienes were studied by several workers,[18] who reported that the polymers formed contained only 6-membered ring units.

Cadogan, Hey and their co-workers[19,20] were the first to study this type of reaction under conditions which led to the formation of mainly monomeric products. They investigated the radical-initiated addition of thiols (Y-Z = H-SR) to ethyl diallylacetate (1,X = $CHCO_2Et$) (Scheme 2.1.I). In a note published recently, they[19] reported that (5,X = $CHCO_2Et$, Y = H, Z = SR) was the only cyclic product formed in the reaction. This means that the radical (2,X = $CHCO_2Et$, Z = SR) cyclizes, exclusively, by attack at the less highly substituted end of the C=C double bond to give the substituted cyclopentylmethyl radical (3,X = $CHCO_2Et$, Z = SR); conversion of (3) to (5) occurs by hydrogen-atom transfer with the thiol (H - SR). They did not detect (6,X = $CHCO_2Et$, Y = H, Z = SR) amongst the products when the reaction mixture was analysed by gas chromatography. They stated that their earlier results,[20] in which the structure (6) was assigned to one of the reaction products, were definitely erroneous.

Brace[21] examined analogous cyclization reactions of radicals produced by the addition of perfluoroalkyl radicals to a number of dienes (1,X = CH_2,O,$CHCO_2Et$,$C(CO_2Et)_2$). (Scheme 2.1.I) In all cases. apart from the expected 1:1 and 2:1 uncyclized adducts, the products obtained are

represented by the structure (5); This shows that cyclization of (2) produced the radical intermediate (3) exclusively. It was also noted that cyclic products were not formed in the reaction of perfluoroalkyl radicals with 1,7-octadiene (1,X = CH_2CH_2) and 1,5-hexadiene. Radical-initiated addition of carbon tetrachloride (Y-Z = Cl-CCl_3) to 1,6-heptadiene (1,X = CH_2) also gave only substituted methylcyclopentane cyclization products including (5,X = CH_2, Y = Cl, Z = CCl_3) and some telomers consisting of only 5-membered ring units.

2.2. CYCLIZATION REACTIONS OF RADICALS FORMED BY ABSTRACTION OF AN ACTIVATED HYDROGEN-ATOM

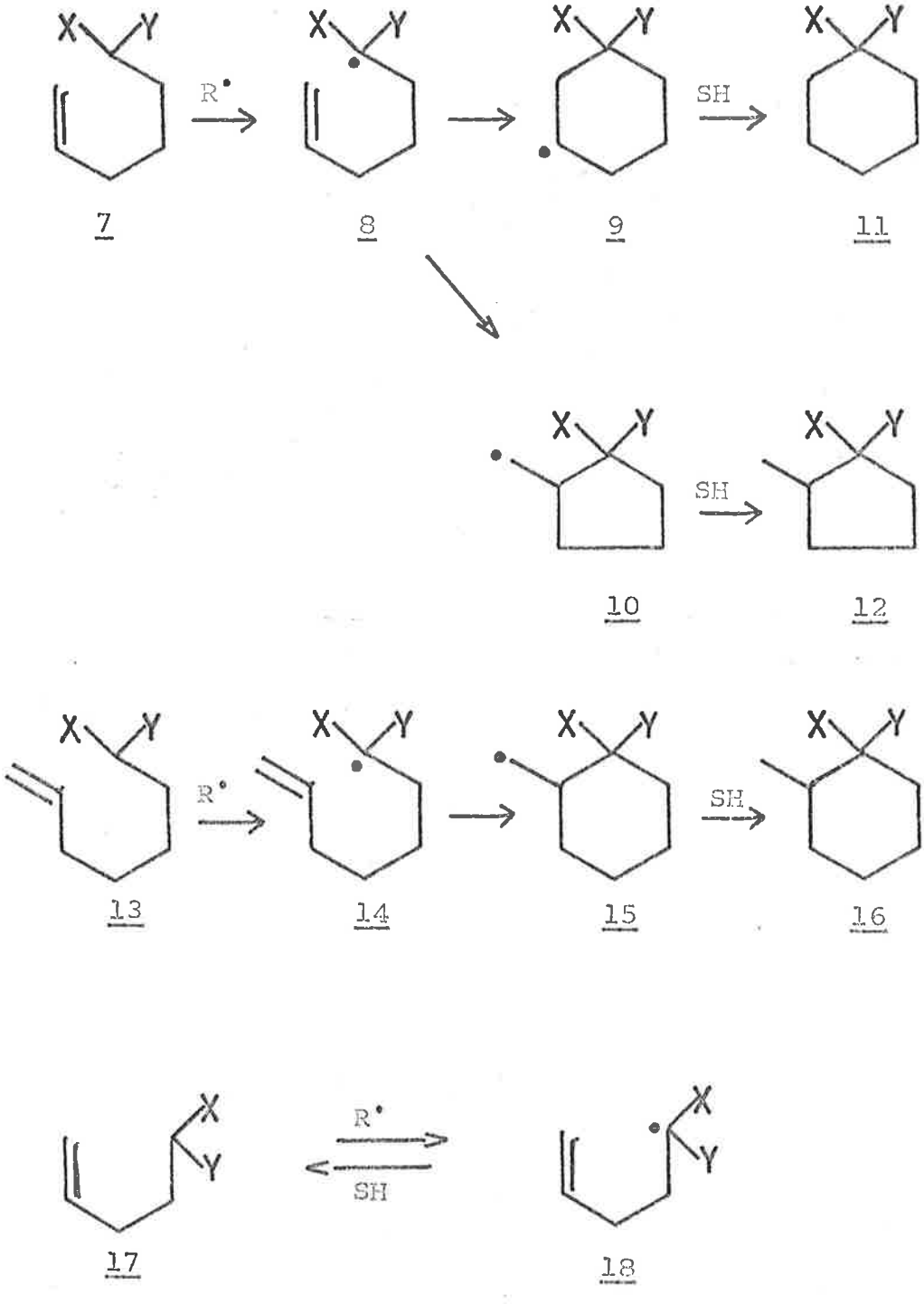
Julia and his collaborators[22-35] have been examining the radical-initiated cyclization reactions of various active methylene compounds containing suitably disposed C=C double bonds. Some simple examples are shown in Scheme 2.2.I.

Julia and Maumy[34] reported that radical (8), formed by hydrogen-atom abstraction from ethyl 2-cyano-6-heptenoate (7), cyclized by attack at either end of the C=C double bond to give the substituted cyclohexyl (9) and cyclopentylmethyl (10) radicals; these radicals were converted to (11) and (12) respectively by hydrogen-atom transfer from the solvent (SH).

They found[27] that the homologous ethyl 2-cyano-7-octenoate (13) was converted to the radical (14) under similar conditions. Cyclization of (14) gave the substituted cyclohexylmethyl radical (15) by attack at the more highly substituted end of the double bond. The product (16) was formed from (15) by hydrogen-atom abstraction from the solvent (S - H). Products arising from attack by radical (14) at the other end of the double bond were not detected.

When subjected to the above reaction conditions, ethyl 2-cyano-4-pentenoate (17) did not give any products that may have arisen from cyclization of radical (18) which must have been present during the course of the reaction.[30]

Key:- X = CN, Y = CO_2Et



Scheme 2.2.I

The mixture of products obtained from the cyclization of radical (8) prompted Julia to examine in detail the reactions of other active methylene compounds in which the double bond is in the 5-6 position relative to the potential radical centre. In their latest papers Julia and Maumy[34,35] discuss, in detail, the factors which influence the relative yields of the substituted cyclohexane and methylcyclopentane products which are formed in these radical cyclization reactions. Furthermore, they found that generation of radical (9) from the appropriate t-butyl perester led to a mixture of the cyclic products (11) and (12). The radical (10) formed in a similar manner also gave a mixture of (11) and (12). On this basis they conclude that both radical cyclization steps are reversible; this is true at least for some of the reactions under consideration. Furthermore they suggest that the two different modes of cyclization, in systems containing a C=C double bond in the 5-6 position relative to the radical centre, can be rationalized in the following manner:-

(i) Generally, radical ring closure is kinetically controlled, favouring 5-membered ring formation.

(ii) The reaction may be brought under thermodynamic control by equilibration of the radical species present. Thermodynamic control, which favours 6-membered ring formation, can be brought into

play be the following factors:

(a) elevated reaction temperatures.

(b) functional groups which stabilize the open-chain radical.

(c) poor hydrogen-atom donating ability of the reaction medium.

Julia and his school explored other aspects of the cyclization reactions of active methylene compounds with suitably disposed double bonds. These included their applications to the synthesis of bicyclic[22-24,27,28,30,31] and tricyclic[29] ring systems as well as to stereoselective synthesis[34] by asymmetric induction. Assignments of the stereochemistry of the bicyclic and tricyclic ring compounds are rather dubious since they employed several degredative steps in the identification procedures. For example they isolated trans-anti-1-decalincarboxylic acid in an overall yield of 7% from the radical cyclization reaction of 2-cyano-5(Δ^1-cyclohexenyl)valeric acid. On this evidence they assigned[27] a trans ring structure for the product of the cyclization reaction.

In 1964 and 1967, Julia[36] reviewed the earlier parts of this work in papers which also summarised some of the other known intramolecular free-radical cyclization reactions.

Recently, Beckwith[37] commented on some aspects of this

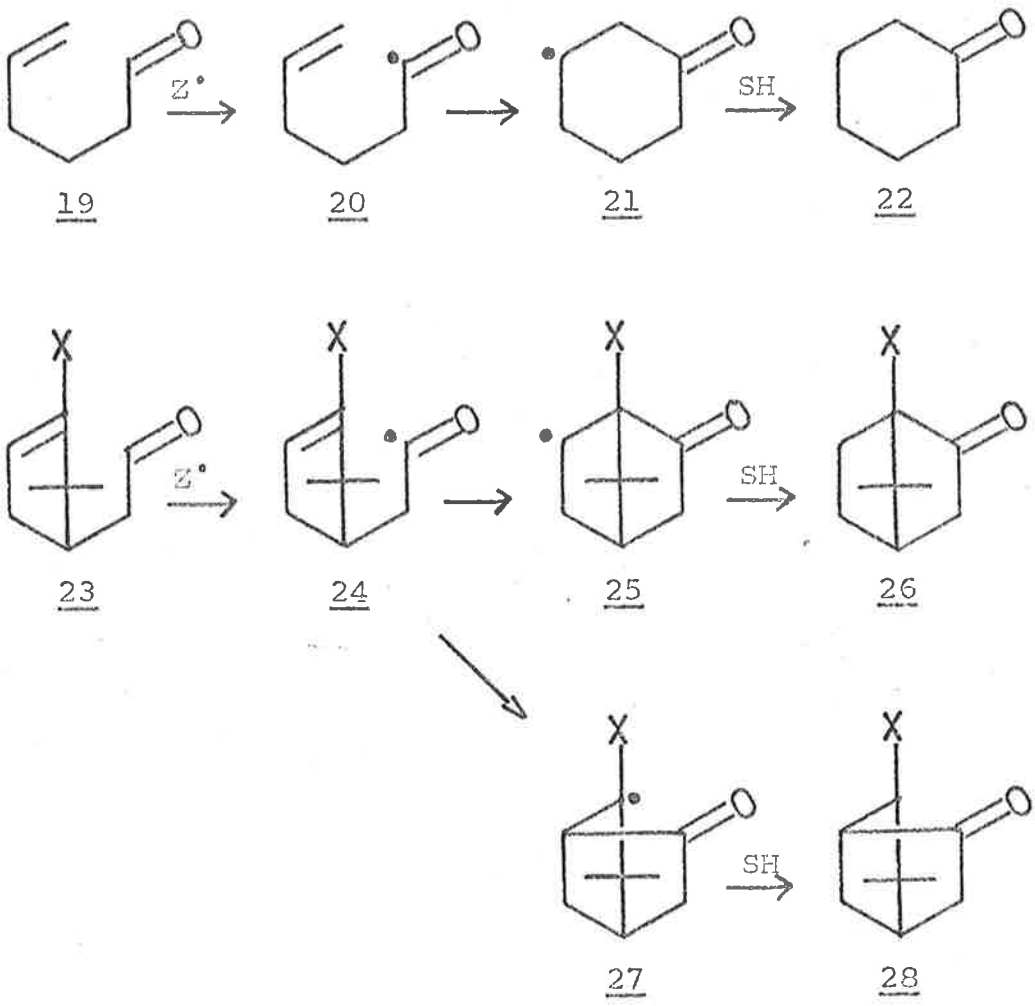
work in his review of radical reactions.

Intramolecular cyclization reactions of aldehydes containing suitably disposed C=C double bonds have been observed in a few instances.

Julia and Maumy[34] found that cyclohexanone (22) was the only cyclic product from the peroxide-initiated reaction of 5-hexenal (19); that is by attack of the acyl radical (20) on the less highly substituted end of the C=C double bond. (Scheme 2.2.II)

Dulou and his co-workers[38] noted that the reaction of 2,2,3-trimethyl-3-cyclopentene-1-acetaldehyde (23,X = CH_3) gave two cyclic products (26,X = CH_3) and (28,X = CH_3) in a ratio of 95:5. This means that formation of the secondary radical (25,X = CH_3) via a 6-membered transition state is favoured over the formation of the tertiary radical (27,X = CH_3) via a 5-membered transition state. (Scheme 2.2.II)

On the other hand, Montheard[39] found that in the analogous reaction of 2,2-dimethyl-3-cyclopentene-1-acetaldehyde (23,X = H), the products (26,X = H) and 28,X = H) were formed in equal yields. In other words, cyclization of the radical (24,X = H) to the secondary radicals (25,X = H) and (27,X = H) via 6-membered and 5-membered transition states respectively are equally facile; assuming equal efficiency of transformations to final products (Scheme 2.2.II).



Scheme 2.2.II

The peroxide-initiated cyclization of citronellal (29) was found[39] to proceed via the 6-membered cyclic radical (31) to give (32) (Scheme 2.2.II). Products arising from the attack of the intermediate radical (30) on the other end of the C=C double bond, resulting in 7-membered ring formation, were not detected.

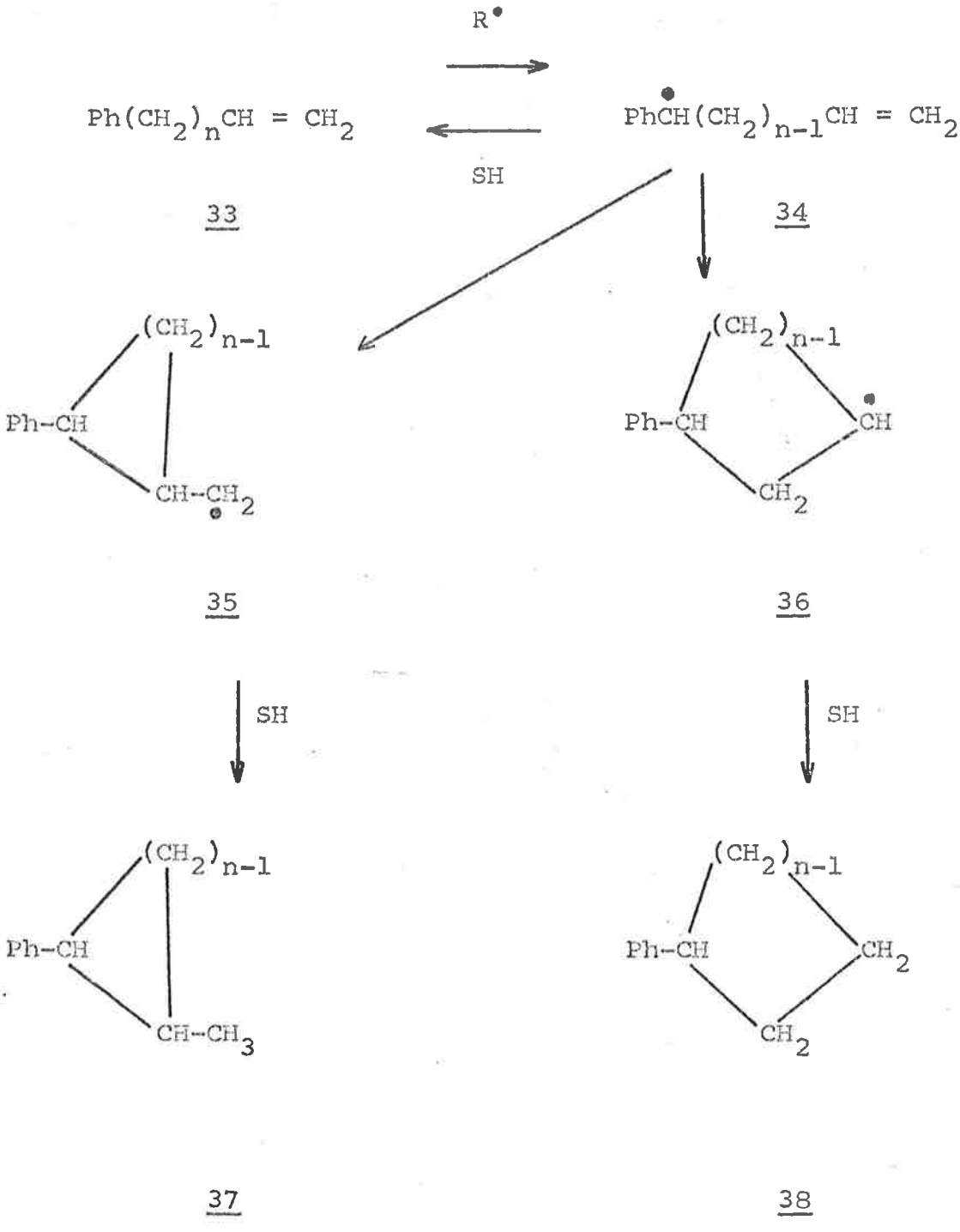
It is interesting to consider the results obtained by Pines and his collaborators[40] who examined the peroxide initiated reactions of a homologous series of ω-phenyl-1-alkenes (33,n = 2,3,4,5) (Scheme 2.2.III). Products obtained only from intramolecular cyclization reactions, leading to monomeric compounds, will be discussed here. They reported the following:

(i) 4-phenyl-1-butene (33,n = 2) did not form any cyclic products.

(ii) 5-phenyl-1-pentene (33,n = 3) formed cyclopentylbenzene (38,n = 3), presumably by cyclization of (34,n = 3) to the radical (36,n = 3).

(iii) 6-phenyl-1-hexene (33,n = 4) gave a mixture of cis- and trans-1-methyl-2-phenylcyclopentane (37,n = 4) by ring closure of (34,n = 4) to (35,n = 4) as well as a relatively smaller amount of phenylcyclohexane (38,n = 4) by alternative cyclization of (34,n = 4) to (36,n = 4).

(iv) 7-phenyl-1-heptene (33,n = 5) produced a mixture



Scheme 2.2.III

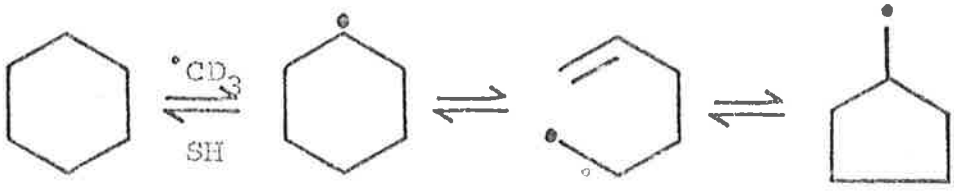
of cis- and trans-1-methyl-2-phenylcyclohexane (37,n = 5) by ring closure of (34,n = 5) to (35,n = 5) as well as a trace amount of cycloheptylbenzene (38,n = 5) by the alternative mode of cyclization of (34,n = 5) to (36,n = 5).

It is to be understood that all the intermediate radical species (35) and (36), mentioned in paragraphs (i) to (iv), were converted to the observed products (37) and (38) respectively by hydrogen-atom transfer with the solvent (SH).

The formation of cyclopentylbenzene from (34,n = 3) represents one of the rare cases of cyclization of a system in which the C=C double bond is in the 4-5 position relative to the radical centre. On the other hand, detection of trace amounts of cycloheptylbenzene, formed from (34,n = 5), is probably the unique example of cyclization by attack at the terminal methylene group of a system in which the double bond is in the 6-7 position relative to the radical centre.

2.3. CYCLIZATION OF ALKYL RADICALS GENERATED IN THE ABSENCE OF STABLIZING FUNCTIONAL GROUPS

Arai and his collaborators[41] found methylcyclopentane amongst the products of the mercury sensitized ultraviolet irradiation of cyclohexane at 400°. They suggested that the cyclohexyl radical (39), formed during the reaction, ring opened to the 5-hexenyl radical (40) which then cyclized to the cyclopentylmethyl radical (41) (Scheme 2.3.I). Methylcyclopentane was formed from (41) by hydrogen-atom transfer with the hydrocarbons present in the reaction mixture.



39 40 41

Scheme 2.3.I

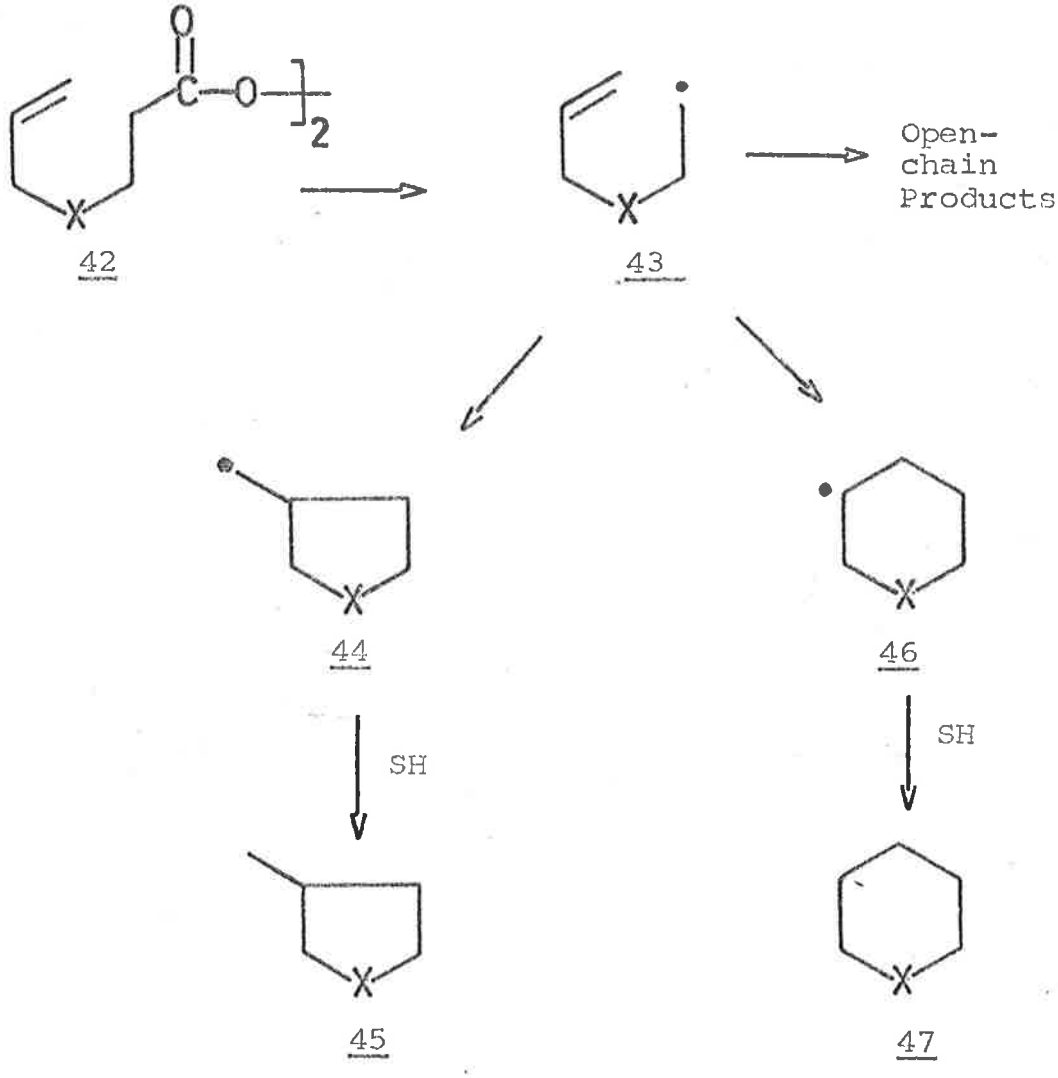
Gordon and his co-workers[42] observed the same rearrangement when they generated the cyclohexyl radical (39) by means of hydrogen-atom abstraction from cyclohexane. They photolized mixtures of perdeuteroacetone and cyclohexane at

various temperatures. They found that with reaction temperatures up to 250° neither methylcyclopentane nor cyclohexane was present in the products. Between 300 and 380° both methylcyclopentane and cyclohexane were formed in significant amounts. At 440° methylcyclopentane was no longer present in the products which contained a much larger amount of cyclohexane. They reasoned that their results indicated rapid reversibility, at high temperatures, of the cyclization of the 5-hexenyl radical (40) to the cyclopentylmethyl radical (41) (Scheme 2.3.I).

Gordon[43] has reviewed this and similar work carried out by his group on the reactions of other cycloalkyl radicals. He noted that the abovementioned rearrangement of a cycloalkyl radical to the appropriate cycloalkylmethyl radical is unique for the cyclohexyl radical, although little work has as yet been done on the reactions of the cycloheptyl radical.

Prompted by the observations of Arai and Gordon a number of workers examined the reactions of the 5-hexenyl radical (40) and related species in which the C=C double bond is in the 5-6 position relative to the carbon radical centre.

Lamb and his co-workers[44] were the first to tackle this problem by examining the decomposition of 6-heptenoyl peroxide (42, $X = CH_2$) (Scheme 2.3.II).



42 43 44 45 46 47

Scheme 2.3.II

They found no kinetic evidence for group participation by the double bond during the thermal decomposition of peroxide (42,X = CH_2). Apart from open-chain products such as 1-hexene and 1,5-hexadiene, three cyclic compounds were detected. Methylcyclopentane (45,X = CH_2) was the major

cyclic product along with small amounts of cyclohexane (47,X = CH_2) and cyclohexene. Generation of cyclopentylmethyl (44, X = CH_2) and cyclohexyl (46, X = CH_2) radicals from cyclopentylacetyl and cyclohexaneformyl peroxides gave only methylcyclopentane and cyclohexane respectively by radical pathways. This showed that both cyclization steps were irreversible under the experimental conditions. They attempted to explain the formation of methylcyclopentane as the major product of the cyclization of the 5-hexenyl radical (43,X = CH_2). Their suggested mechanism involved the initial formation of an intramolecular complex between the radical centre and the double bond followed by hydrogen-atom transfer from the solvent. This mechanism, by its nature, excludes the intermediacy of free cyclopentylmethyl and cyclohexyl radicals in the reaction.

Lamb and his collaborators[45] also investigated the decomposition of 3-allyloxypropionyl peroxide (42,X = 0) (Scheme 2.3.II). They found that the only cyclic product produced in the reaction was 3-methyltetrahydrofuran (45, X = 0). This was formed by cyclization of the 2-allyloxyethyl radical (43,X = 0) to the 5-membered ring radical (44,X = 0) followed by hydrogen-atom transfer from the solvent.

It was established by Walling and Rabinowitz[46] that alkyl radicals are formed by a chain process in the reactions of

trialkyl phosphites with mercaptans. Using this process, Walling and Pearson[47] generated 5-hexenyl and 4-pentenyl radicals from 1-mercapto-5-hexene and 1-mercapto-4-pentene respectively. At low temperatures methylcyclopentane was the major product from the reactions of the 5-hexenyl radicals; 1-hexene was the other product. At higher temperatures a very small amount of cyclohexane was also detected in the reaction mixture along with the abovementioned products. Reactions in which 4-pentenyl radicals were generated did not give any cyclic products. The authors suggested that, from inspection of molecular models, it was not very surprising that the 4-pentenyl radical did not cyclize. The reason given was that in the intramolecular attack on the double bond the transition state is highly strained. They explained the formation of methylcyclopentane from the 5-hexenyl radical as being due to a steric factor, but did not elaborate further on this point.

Weedon and his collaborators[48] found that 1,2-dicyclopentylethane and 1-cyclopentyl-6-hexene were the only products formed by Koble electrolysis of 5-heptenoic acid. They suggested that some of the 5-hexenyl radicals, formed during the reaction, cyclized to cyclopentylmethyl radicals before radical coupling occurred to give the observed products. No compounds arising from cyclohexyl radicals were found.

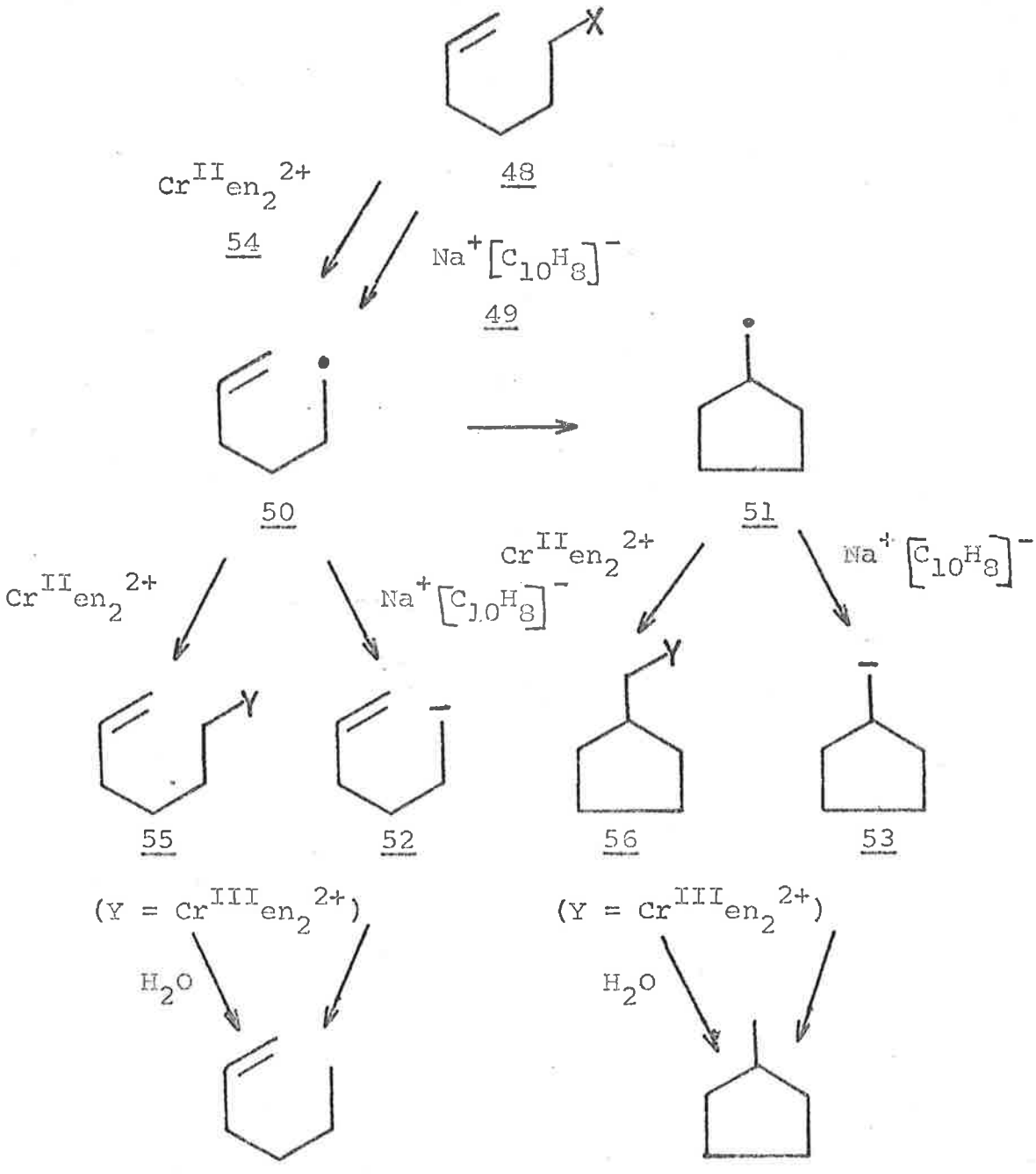
When subjected to the same treatment, cyclopentylacetic and cyclohexanecarboxylic acids both gave the expected products by Kolbe coupling without ring opening of the intermediate cyclopentylmethyl and cyclohexyl radicals; hence they concluded that both radical cyclization reactions were irreversible under these conditions. Electrolysis of 5-hexenoic and 7-octenoic acids did not give any products resulting from cyclization of the intermediate 4-pentenyl and 6-heptenyl radicals respectively.

Evidence for free radical formation by one-electron oxidation of Grignard reagents was furnished by Kharasch.[49]

Lamb and his co-workers[50] isolated a mixture of 5-hexenol and cyclopentyl carbinol from the reaction of 5-hexenylmagnesium bromide with molecular oxygen. They reasoned that some of the 5-hexenyl radicals, generated by one-electron oxidation of the Grignard complex, were able to cyclize cyclopentylmethyl radicals before rapid interception of both radical species by molecular oxygen. Cyclohexanol was not detected in the reaction mixture; this excluded the intermediacy of cyclohexyl radicals in the reaction. Cyclopentyl carbinol was the only product of the reaction of cyclopentylmagnesium bromide with molecular oxygen; this demonstrated the irreversibility of the radical cyclization step under these conditions.

Lamb[51] also generated 5-hexenyl radicals (50) by one-electron reduction of 5-hexenyl chloride (48,X = Cl) and 5-hexenyl bromide (48,X = Br) with sodium naphthalene (49) (Figure 2.3.III). Some of the 5-hexenyl radicals (50) cyclized to cyclopentylmethyl radicals (51) before both (50) and (51) were reduced by excess sodium naphthalene (49) to the anionic species (52) and (53) respectively. Protonation of the anions (52) and (53), by the solvent, gave 1-hexene and methylcyclopentane, the observed products. The possibility of an anionic mechanism for the cyclization step was ruled out by the fact that cyclic products were not formed when a large excess of sodium naphthalene (49) was used. The reaction of cyclopentylmethyl bromide with (49) to give methylcyclopentane as the only C_6 hydrocarbon, showed that the radical cyclization step was irreversible under the experimental conditions.

Recently it was reported, by Kochi and Powers,[52] that alkyl halides are reduced quantitatively by an ethylene-diaminechromium(II) reagent (54) (Scheme 2.3.III). For example, the reaction proceeds with very rapid bromine-atom transfer from 5-hexenyl bromide (48,X = Br) to the chromium reagent (54) to give 5-hexenyl radicals (50). Some of the 5-hexenyl radicals cyclize to cyclopentylmethyl radicals (51). This cyclization reaction competes with the rapid trapping of (50) by (54) to give the organometallic chromium (III) complex



Scheme 2.3.III

(55). Similarly (51) is trapped to give (56). Aqueous hydrolysis of the chromium (III) complexes (55) and (56) gives 1-hexene and methylcyclopentane in quantitative combined yield. The formation of methylcyclopentane is favoured over that of 1-hexene at low concentrations of the chromium reagent (54). Cyclohexane is not formed in the reaction. Irreversibility of the cyclization step under the reaction conditions is demonstrated by reduction of cyclopentylcarbinyl bromide with (54) to give methylcyclopentane in a quantitative yield. The reaction of (54) with 6-heptenoyl peroxide gives similar results to those obtained for (48,X = Br); this shows the versatility of the chromium reagent (SH).

2.4. CYCLIZATION OF ALKYL RADICALS GENERATED FROM ALKYL HALIDES BY TRIALKYL AND TRIARYL STANNANES

Kuivila[53] in his review of the reactions of stannanes described the free-radical chain mechanism which was postulated for the reduction of alkyl halides by trialkyl and triaryl stannanes when initiated by a radical source.

Subsequently, Menapace and Kuivila[54] presented further experimental evidence in support of the free-radical chain mechanism of these reactions.

Detailed kinetic investigation of the photo-initiated reduction of alkyl halides by tri-n-butylstannane was carried out by Carlsson and Ingold[55] using a calorimetric method in conjunction with the rotating sector technique. They confirmed the two-step free-radical chain mechanism for these reactions from the kinetic data which they obtained. The mechanism is shown in Scheme 2.4.I.

Initiation

$\longrightarrow$ $R^{\bullet}$

Propagation

$R^{\bullet} + R'_3SnH \longrightarrow RH + R'_3Sn^{\bullet}$

$R'_3Sn^{\bullet} + RX \longrightarrow R'_3SnX + R^{\bullet}$

Termination

$R^{\bullet} + R^{\bullet} \longrightarrow$

$R^{\bullet} + R'_3Sn^{\bullet} \longrightarrow$ Inactive Products

$R'_3Sn^{\bullet} + R'_3Sn^{\bullet} \longrightarrow$

Scheme 2.4.I

They were able to determine the absolute rate constants of these reactions, however the mathematical treatment which they put forward will not be dealt with here. Suffice to say that the reduction of alkyl halides with stannanes generally exhibited straight-forward kinetics. The following points emerge from their work:

(i) The rate usually shows first-order dependence on either the alkyl halide or the stannane concentration over a wide range of relative and absolute reactant concentrations.

(ii) The reactions behave normally throughout their entire course, continuing until one of the reactants is completely consumed.

(iii) For the reactions of alkyl bromides and methyl iodide, chain termination must occur by self reaction of two alkyl radicals; the rate controlling step is hydrogen-atom abstraction from the stannane.

(iv) For the reductions of alkyl chlorides chain termination must involve the coupling of two stannyl radicals; the rate controlling step is chlorine atom abstraction from the alkyl chloride.

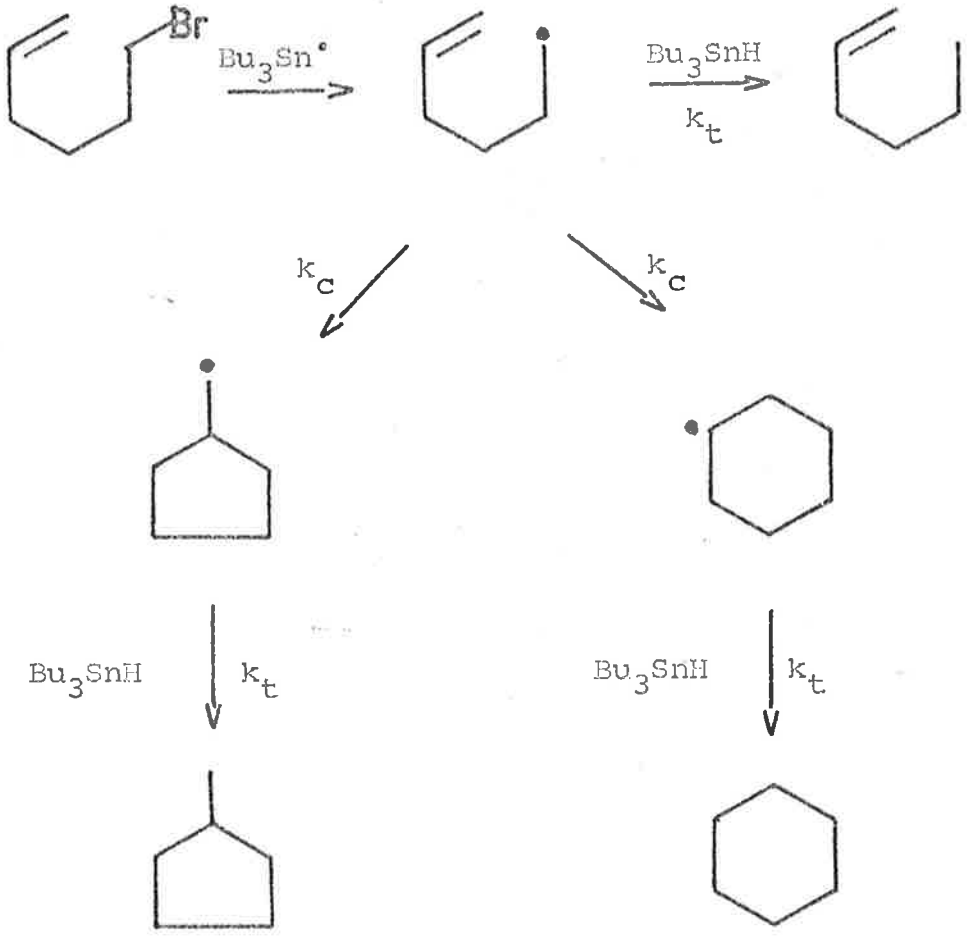
(v) The relative reactivities of alkyl halides towards tri-n-butyltin radicals, measured in a series of competitive experiments, vary from the arbitrary value of 1 assigned to 1-chloropentane, through

19,000 for n-hexyl bromide, up to 2,090,000 for methyl iodide.

(vi) Rates of hydrogen-atom abstraction by alkyl radicals from tri-n-butylstannane show only a small increase in the order:- t-butyl<n-hexyl ≤cyclohexyl<methyl. The value obtained from the reduction of n-hexyl bromide may be taken as the average value of the rate constant for hydrogen-atom abstraction ($1 \times 10^6 M^{-1} sec^{-1}$). This value of k_t can be used to estimate the rate constants of such alkyl radical isomerization reactions in which the rate constants of hydrogen-atom abstraction from tri-n-butylstannane are approximately the same for all the isomeric radical species.

The authors then demonstrated how the above principles can be applied to previously reported radical isomerization reactions by the groups of Walling[56] and Beckwith[57]; these are reported below.

Walling[56] and his co-workers investigated the reaction of 5-hexenyl bromide with tri-n-butylstannane at various stannane concentrations. They reported that the reaction gave 1-hexene and methylcyclopentane in relative ratios that were dependent on the stannane concentration. Very small amounts of cyclohexane were also formed. (Scheme 2.4.II)



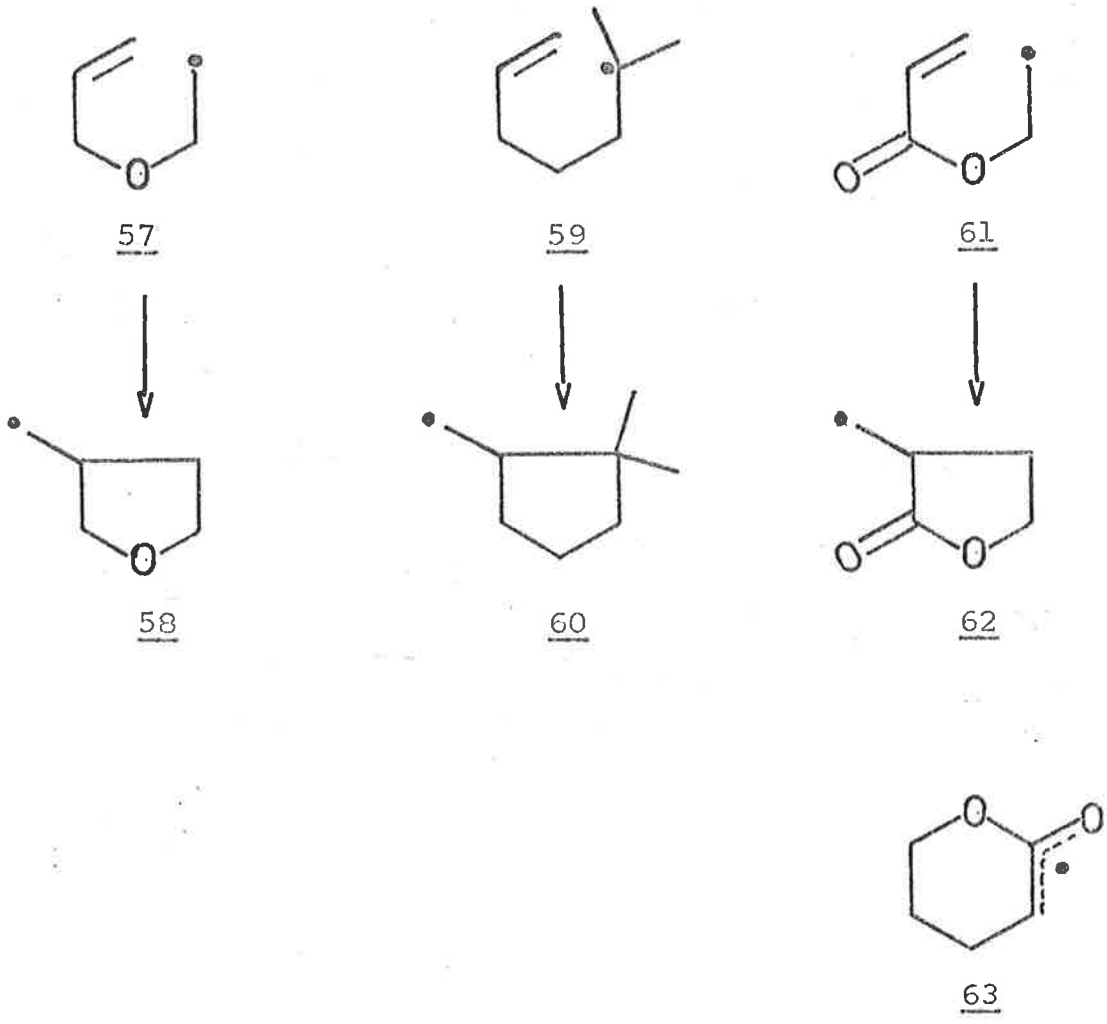
Scheme 2.4.II

The reduction of cyclopentylmethyl bromide and bromocyclohexane, using the same procedure, gave only methylcyclopentane and cyclohexane respectively; this showed that both cyclization steps were irreversible under the reaction conditions. They proposed two separate kinetic schemes to

explain the preferred formation of methylcyclopentane over that of cyclohexane. One of these schemes involved the formation of an intramolecular complex between the radical centre and the π-bond, and subsequent reaction of this intermediate with the stannane to give methylcyclopentane. They concluded, however, that neither scheme satisfied all the experimental results.

Using the reduction of the appropriate bromo compound with tri-n-butylstannane, these workers[56] investigated several other radical reactions. These may be classified into three distinct groups according to the position of the C=C double bond in relation to the radical centre:-

(i) In the first group of compounds, the double bond was in the 5-6 position relative to the radical centre. Apart from the expected open-chain compounds, radicals (57), (59) and (61) gave 3-methyltetrahydrofuran, 1,1,2-trimethylcyclopentane and a γ-lactone respectively. Presumably, the cyclic products were formed by ring closure of radicals (57), (59) and (61) via 5-membered transition states to the cyclic radicals (58), (60), and (62) respectively (Scheme 2.4.III). It is interesting to note that products arising from the alternative mode of cyclization, that is via 6-membered transition states, were not observed.



Scheme 2.4.III

The radical (61) would form the resonance stabilized species (63) by this alternative process.

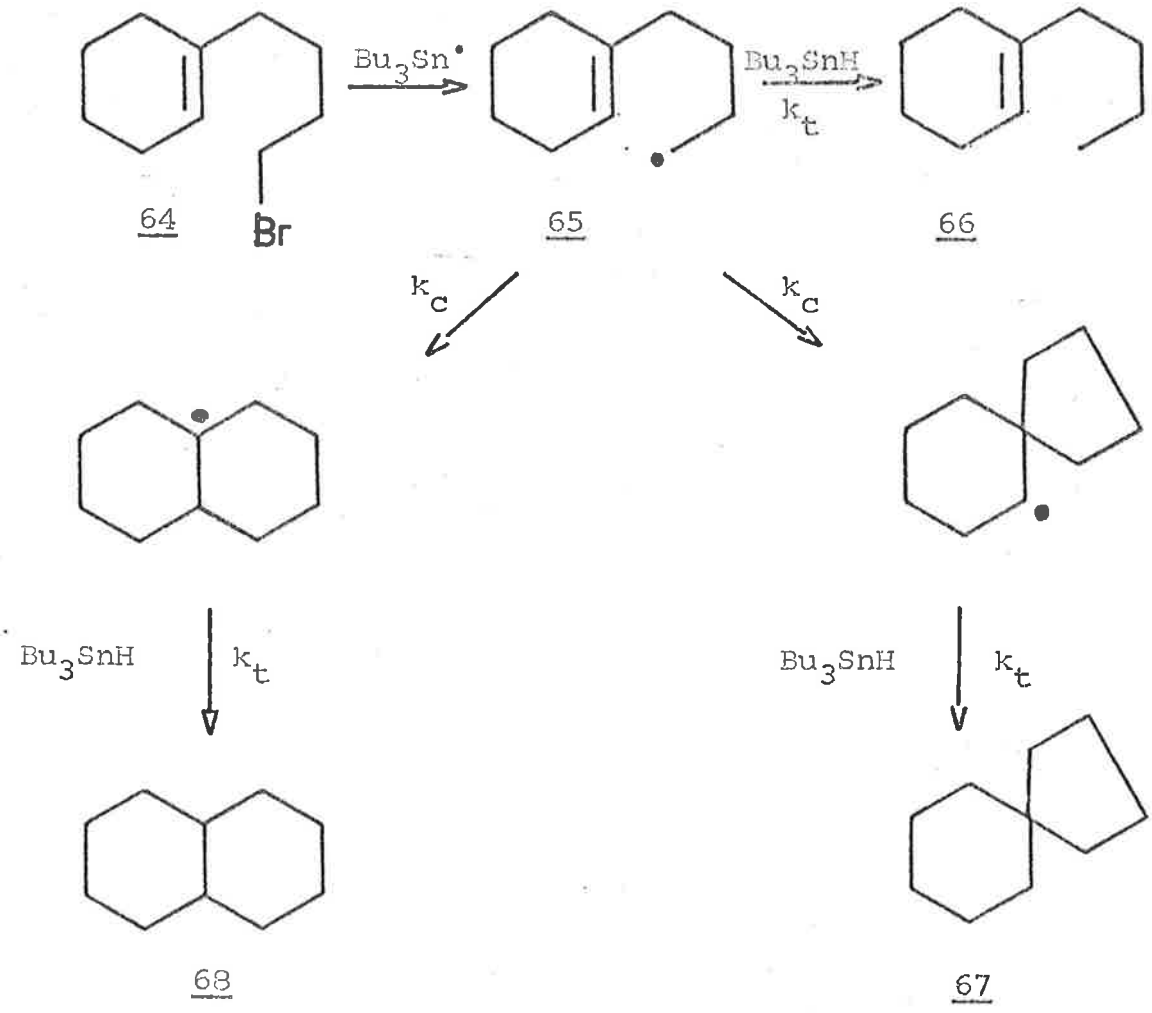
(ii) & (iii) Cyclic products were not formed in the reactions of the second and third group of compounds in which the double bonds were in the 4-5 and 6-7 positions, respectively, in relation to the

potential radical sites; open chain reduced products were formed in these cases.

For the abovementioned reactions of 6-bromo-1-hexene with tri-n-butylstannane, Carlsson and Ingold[55] calculated the ratio of the rate constant of cyclization (k_c) and the rate constant of hydrogen-atom abstraction (k_t) from the relative yields of methylcyclopentane and 1-hexene at various stannane concentrations. The value they obtained for k_c/k_t was 0.1. The average value of k_t was shown[55] to be $1 \times 10^6 M^{-1} sec^{-1}$, hence k_c was estimated to be $10^5 sec^{-1}$ for this reaction.

Struble, Beckwith and Gream[57] reported that the reaction of 4-(Δ^1-cyclohexenyl)butyl bromide (64) with tributylstannane gave a mixture of 1-butylcyclohexene (66), 1,1-tetramethylenecyclohexane (67), cis- and trans-decalin (68) (Scheme 2.4.IV). It is noteworthy that throughout the wide range of stannane concentrations used in the various runs, the combined yields of cis- and trans-decalins (68), arising from the cyclization of radical (65) via a 6-membered transition state, were of the same order as the yield of the spiro compound (67), which arose from ring closure of (65) via a 5-membered transition state. They proposed that the initial stages of the radical addition involve interaction of the unpaired electron with the lowest unoccupied orbital of the

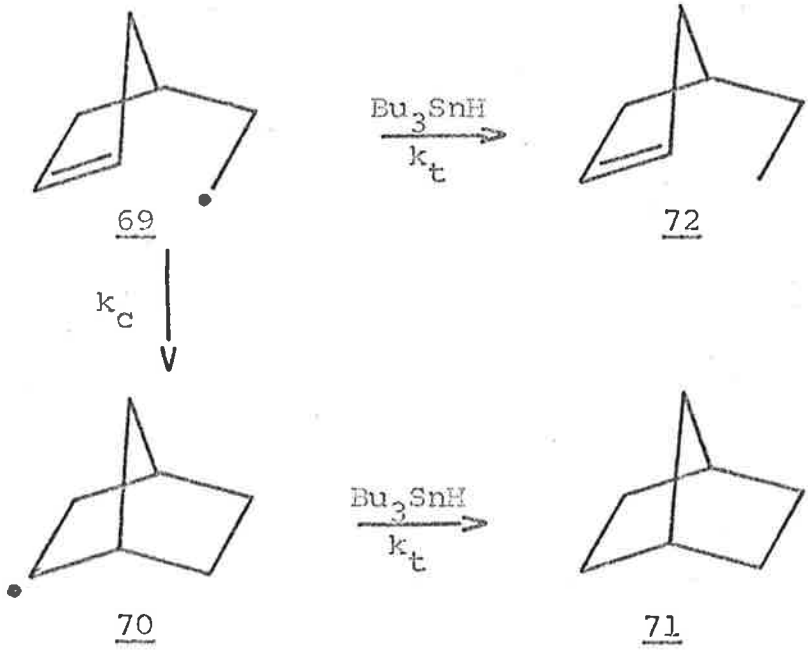
π- system, and that the approach of the radical centre occurs preferably within the plane of the π- system and along a line extending almost vertically from one of the terminal carbon atoms. Furthermore, they suggested that this scheme rationalizes not only the preferred formation of 5-membered rings, but also the cyclization of 6-heptenyl systems and the inability of the 4-pentenyl system to undergo ring formation.



Scheme 2.4.IV

Carlsson and Ingold[55] calculated k_c/k_t for the above reaction to be 4×10^{-2}. Since k_t was shown to be $1 \times 10^6 M^{-1}sec^{-1}$, they estimated k_c for the 4-(Δ^1-cyclohexenyl)butyl radical to be $4 \times 10^4 sec^{-1}$.

Wilt and his collaborators[58] recently studied the reaction of the 2-(Δ^3-cyclopentenyl)ethyl radical (69) formed from 2-(Δ^3-cyclopentenyl)ethyl bromide by reduction with tributylstannane. (Scheme 2.4.V)



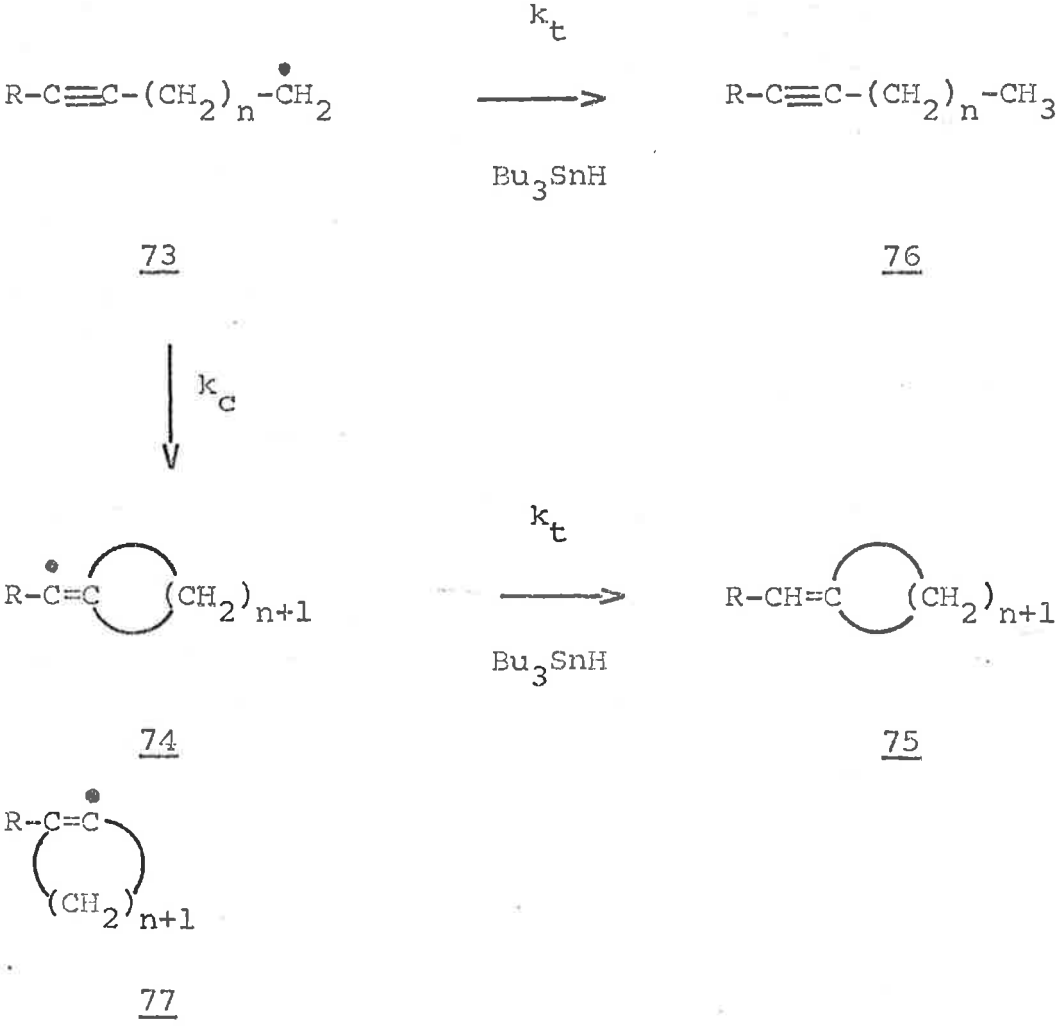
Scheme 2.4.V

The radical (69) was found to give norbornane (71) by cyclization to the norbornyl radical (70) followed by hydrogen-atom abstraction, as well as 4-ethylcyclopentene

(72) by direct hydrogen-atom transfer with the stannane. The ratios of the yields of (71) and (72) were determined at various stannane concentrations at three different temperatures. At 40°, only traces of norbornane (71) were formed showing that cyclization of (69) to(70) is much slower than that of the analogous 5-hexenyl radical.[56] At 93° and at 130° (71) represented only 20% and 41% of the reduced products respectively. They[58] calculated the rate constants of cyclization by the method of Carlsson and Ingold[55] and obtained the values 1.9×10^{4} and 7.3×10^{3} for the reaction at 130° and 93° respectively. It should be noted that the radical (69) is symmetrical, so that attack at either end of the double bond yields the same radical intermediate (70) via a 5-membered transition state. Intrinsic steric strain in the norbornyl radical (70) and hence strain in the transition state leading to its formation was put forward as the reason for the low yields of norbornane (71) obtained. They supported the suggestions by Beckwith and his co-workers[57] concerning the likely transition state for intramolecular radical cyclization reactions.

Recently Crandall and Keyton[59] investigated the reactions of radicals generated by tributylstannane from bromo and chloro acetylenes. They examined the effect of the distance of the triple bond from the radical centre, as well as the

influence of terminal substituents on the reactions of these systems. The radicals under investigation are shown in a general form by (73) (Scheme 2.4.VI).



Scheme 2.4.VI

They found that:-

(i) The radicals (73, n=1,2; R=C_6H_5) gave only open-chain products (76, n=1,2; R=C_6H_5).

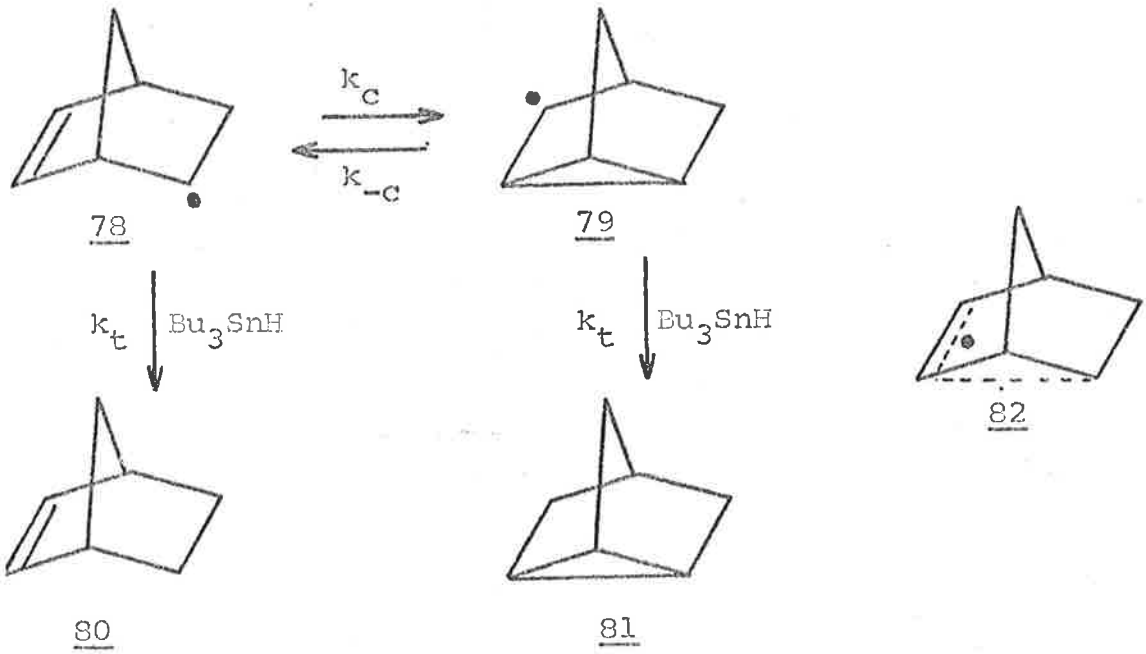
(ii) The radicals (73, n=3, R=C_6H_5, C_5H_{11}) cyclized only to the 5-membered ring radical intermediates (74,

n=3; R=C_6H_5, C_5H_{11}) yielding the cyclopentylmethylene compounds (75, n=3; R=C_6H_5, C_5H_{11}). No products via the alternative 6-membered ring radical intermediate (77, n=3; R=C_6H_5, C_5H_{11}) were formed.

(iii) The most interesting observations came from the reactions of the radicals (73, n=4). In particular, (73, n=4; R=C_6H_5) gave a mixture of two products which were (75, n=4; R=C_6H_5) and (76, n=4; R=C_6H_5). The highest ratio of (75):(76) which they obtained was 3:1. In strong contrast, the analogous radical (74, n=4; R=C_5H_{11}) did not give any cyclic products but yielded (76, n=4; R=C_5H_{11}) nearly quantitatively. The authors suggested that the likely explanation for the difference in the reactions of the two radicals (73, n=4; R=C_6H_5) and (73, n=4; R=C_5H_{11}) was the fact that mesomeric stabilization was possible only in the intermediate radical (74, n=4; R=C_6H_5) arising from the cyclization of (73, n=4; R=C_6H_5).

The cyclization reactions discussed so far in this section were considered to be irreversible under the reaction conditions that were employed. Kuivila and his co-workers,[60] however, found one particular reaction in which the rate of radical

cyclization and the rate of radical ring opening were of the same order. This observation came from their investigations into the possibility of the transient existence of the non-classical norbornyl radical (82) (Scheme 2.4.VII).



Scheme 2.4.VII

They noted that the same mixture of norbornene (80) and nortricyclene (81) resulted from the reduction of both norbornenyl bromide and nortricyclyl bromide with tributyl-stannane. This means either that both reactions proceed through a common intermediate such as the non-classical radical (82) or that the two radical intermediates (78) and (79) are in rapid equilibrium. When triphenylstannane was used for the reduction of nortricyclyl bromide, they found

that the relative yields of (80) and (81) were dependent on the stannane concentration. This observation discounts the possible intermediacy of the non-classical radical (82), since from such a species the relative yields of (80) and (81) should not be influenced by variations in the stannane concentration. The rate constant of hydrogen-atom transfer from triphenylstannane to alkyl radicals is larger than that from tributylstannane; thus triphenylstannane in high concentrations is able to intercept most of the nortricyclyl radicals (79), formed from nortricyclyl bromide, before ring opening to the norbornenyl radical (78) can occur. The conversion of (78) to (79) is one of the few examples of cyclization in a system containing a C=C double bond in the 4-5 position relative to the radical centre.

CHAPTER 3

HOMOLYTIC AROMATIC SUBSTITUTION

3.1. INTERMOLECULAR AROMATIC SUBSTITUTION REACTIONS OF ARYL RADICALS

The intermediacy of aryl radicals in certain aromatic substitution reactions was first proposed by Grieve and Hey[61]. They noted that the similar directive effects of electron-withdrawing and electron-donating substituents on the pattern of arylation of various benzene derivatives did not comply with the established patterns of either electrophilic or nucleophilic aromatic substitution reactions. Subsequent work carried out in this field has been extensively reviewed by Williams[62], Hey[63,64] and the Intra-Science Symposium[65].

3.2. INTRAMOLECULAR AROMATIC SUBSTITUTION REACTIONS OF ARYL RADICALS

The synthetic utility and the theoretical problems associated with intramolecular homolytic aromatic substitution reactions made them the subject of varied investigations. Reviews on this topic were compiled by Abramovitch[66], Hey[64] and by the Intra-Science Symposium[65].

CHAPTER 4

DETECTION OF RADICALS BY ELECTRON PARAMAGNETIC RESONANCE SPECTROSCOPY

4.1. STATIC SYSTEMS

Electron paramagnetic resonance (e.p.r.) techniques have been used widely for the observation of e.p.r. spectra of stable organic and inorganic radicals. A number of textbooks and reviews have been written on the theory and practical applications of e.p.r. spectroscopy[67-74].

As in all forms of spectroscopy a certain minimum concentration of the species under investigation is required for the successful observation of its spectrum. This requirement is easily met by stable radicals which have long lifetimes, but it is the stumbling block for the observation of many transient organic radicals. In other words if the radicals are formed slowly and destroyed rapidly or formed and destroyed rapidly there will not be a sufficient stationary concentration of the radical species to record its e.p.r. spectrum.

Fessenden and Schuler[75] were the first to observe the e.p.r. spectra of transient alkyl radicals. They used high energy gamma-irradiation to generate alkyl radicals from a number of hydrocarbons in the cavity of the e.p.r. spectrometer. Their results provided detailed structural and kinetic information about alkyl radicals. The narrowness of the spectral lines allowed accurate determinations of the hyperfine structure of the spectra which they were able to record. The

following generalizations may be made as a result of their observations:-

(i) All alkyl and cycloalkyl radicals have α-coupling constants at 21 to 23 gauss, excepting the cyclopropyl radical.

(ii) In cases where isotropic rotational averaging is possible, the β-coupling constants decrease with increasing substitution on the α-carbon-atom and are represented by the values observed for the methyl protons in ethyl (26.87 gauss), isopropyl (24.68 gauss) and t-butyl(22.72 gauss). radicals.

(iii) Some β-coupling constants are different from the values mentioned in (ii) and are temperature dependent. These anomalies are attributed to hindered rotation about the α-β carbon-carbon bond, which prevent isotropic averaging.

(iv) Small splitting by the γ-protons (0.4 - 1.1 gauss) can be resolved in some cases. Substantial angular dependance of these coupling constants are documented in the case of propyl radicals.

(v) The smaller α-coupling constants observed for the vinyl and cyclopropyl radicals can be interpreted as being due to the increased s-character of the orbital in which the unpaired electron resides.

(vi) The value of the g-factor which defines the position of the centre of the absorption pattern is close to the free-spin value of 2.0023 for all simple alkyl radicals.

Kochi and Krusic[76] reported a convenient method of generating alkyl radicals in the cavity of the e.p.r. spectrometer by ultraviolet irradiation of acyl peroxides in hydrocarbon solvents such as cyclopropane. Of particular interest are the spectra which they obtained from the photolysis of 6-heptenoyl peroxide at various temperatures. At -75° the spectrum of the 5-hexenyl radical was observed, whilst at -35° only the spectrum of the cyclopentylmethyl radical formed from cyclization of the 5-hexenyl radical was recorded. At intermediate temperatures superimposed spectra of the above two radicals were obtained. Cyclopentylacetyl peroxide was irradiated at various temperatures up to 0° but only the spectrum of the cyclopentylmethyl radical was observed; this showed once again that cyclization of the 5-hexenyl radical was not reversible under these conditions. They also recorded the spectra of 3-butenyl and 5-pentenyl radicals, which apparently did not cyclize under these experimental conditions.

Krusic and Kochi[77] recently recorded the e.p.r. spectra

of a series of alkyl radicals substituted in the β position with sulphur, silicon, germanium and tin groups. They found that the hyperfine isotropic coupling constants for the β protons were unusually small and exhibited considerable temperature dependence. They interpreted these results in terms of hindered internal rotation about the $C_\alpha - C_\beta$ bond and a preferred conformational orientation in these radicals in which the sulphur, silicon, germanium and tin atoms are eclipsed with the p-orbital at the trigonal radical centre. The conformational effects were attributed to incipient 1,3-bonding between the unfilled 3d orbitals of the hetero-atom and the p-orbital of the carbon radical centre. The authors ruled out structures involving symmetrically bridged radicals. They also determined the barrier heights of hindered rotation by the classical treatment; these were about 2 kcal/mole for the heterosubstituted radicals, whereas the value for the isobutyl radical was only 0.3 kcal/mole.

4.2. THE FLOW TECHNIQUE

The flow technique is used for observation of the e.p.r. spectra of transient radicals generated in solution. This topic was discussed recently by Beckwith.[74]

Using this method, Beckwith and Norman[78] observed the e.p.r. spectra of organic radicals generated by the one-electron reduction of aliphatic halogeno compounds in aqueous solution. They[79] attempted unsuccessfully to observe the e.p.r. spectra of phenyl and substituted phenyl free-radicals formed by the one-electron reduction of the appropriate aryldiazonium salts. On the other hand, they[79] were able to record the spectra of the radical intermediates formed by addition of these aryl radicals to various olefinic, acetylenic, aromatic and inorganic substrates in both acidic and alkaline media.

Recently Beckwith[74] reported the e.p.r. spectra of two ortho-substituted aryl free-radicals using the flow technique. The values which he recorded for the ortho, meta and para coupling constants and the value of the g tensor were similar to those obtained by Kasai and his collaborators[80] for the phenyl radical trapped in an argon matrix.

PART II

CHAPTER 5

RESULTS AND DISCUSSION

OBJECTIVES

Our initial aim was to determine if aryl radicals substituted in the ortho-position with sidechains containing terminal C=C double bonds in the 5-6 or 6-7 position relative to the radical centre would undergo intramolecular ring closure reactions. With this in mind we investigated the suitability of electron paramagnetic resonance spectrometry for the detection of possible radical intermediates in these reactions.

When we had succeeded to detect, by e.p.r. spectrometry, cyclic radical intermediates in the reactions of three such aryl radicals, we decided to develop a general technique which would make it possible to generate and to study the products from a number of aryl radicals suitable for the proposed investigations. Our main aims from such product studies were:-

(i) To ascertain if the well documented specificity of most alkyl radicals, containing suitably disposed double bonds, to undergo ring closure predominantly or even exclusively at one particular carbon-atom of the respective C=C double bonds would be exhibited also by aryl radicals.

(ii) To estimate the rate constants of cyclization of these aryl radical reactions.

(iii) To observe what effect the inclusion of a

heteroatom, such as oxygen or nitrogen in that part of the respective sidechains which links the terminal C=C double bond with the benzene ring, would have on the rate and course of these cyclization processes.

5.1. ELECTRON PARAMAGNETIC RESONANCE STUDIES

The recently developed method of generating aryl radicals in the cavity of an e.p.r. spectrometer, by one-electron reduction of aryldiazonium salts with titanium (III) ethylenediaminetetraacetic acid complex in a flow cell,[79] was used to observe the spectra of radicals generated from o-allyloxybenzenediazonium borofluoride (83a), o-(2-methylallyloxy)benzenediazonium borofluoride (83b) and o-(3-butenyloxy)benzenediazonium borofluoride (83c). (Scheme 5.1.I) The resultant spectra are shown in Figures 5.1.I, 5.1.II and 5.1.III respectively. Figures 5.1.I and 5.1.III depict doublets of triplets, whereas Figure 5.1.II shows a triplet. Characteristics of these spectra are shown in Table 5.1.I.

Diazonium Salt	Coupling Constants			g-value
	$a_{H\alpha}$	$a_{H\beta}$	$a_{H\gamma}$	
83a	22.2	19.0	1.0	2.0025
83b	20.4	-	-	2.0023
83c	21.3	26.2	-	2.0025

Table 5.1.I

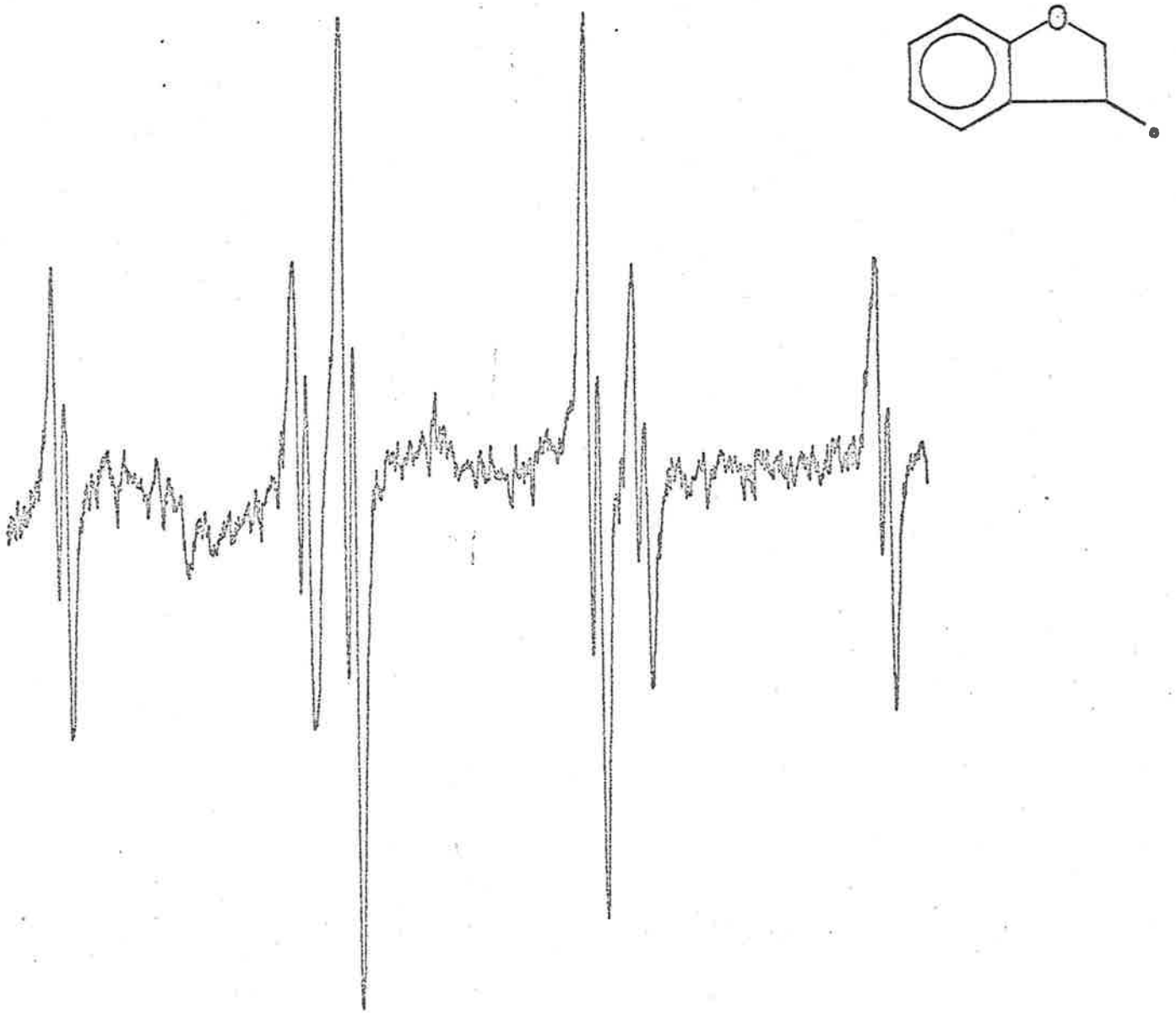


Figure 5.1.I

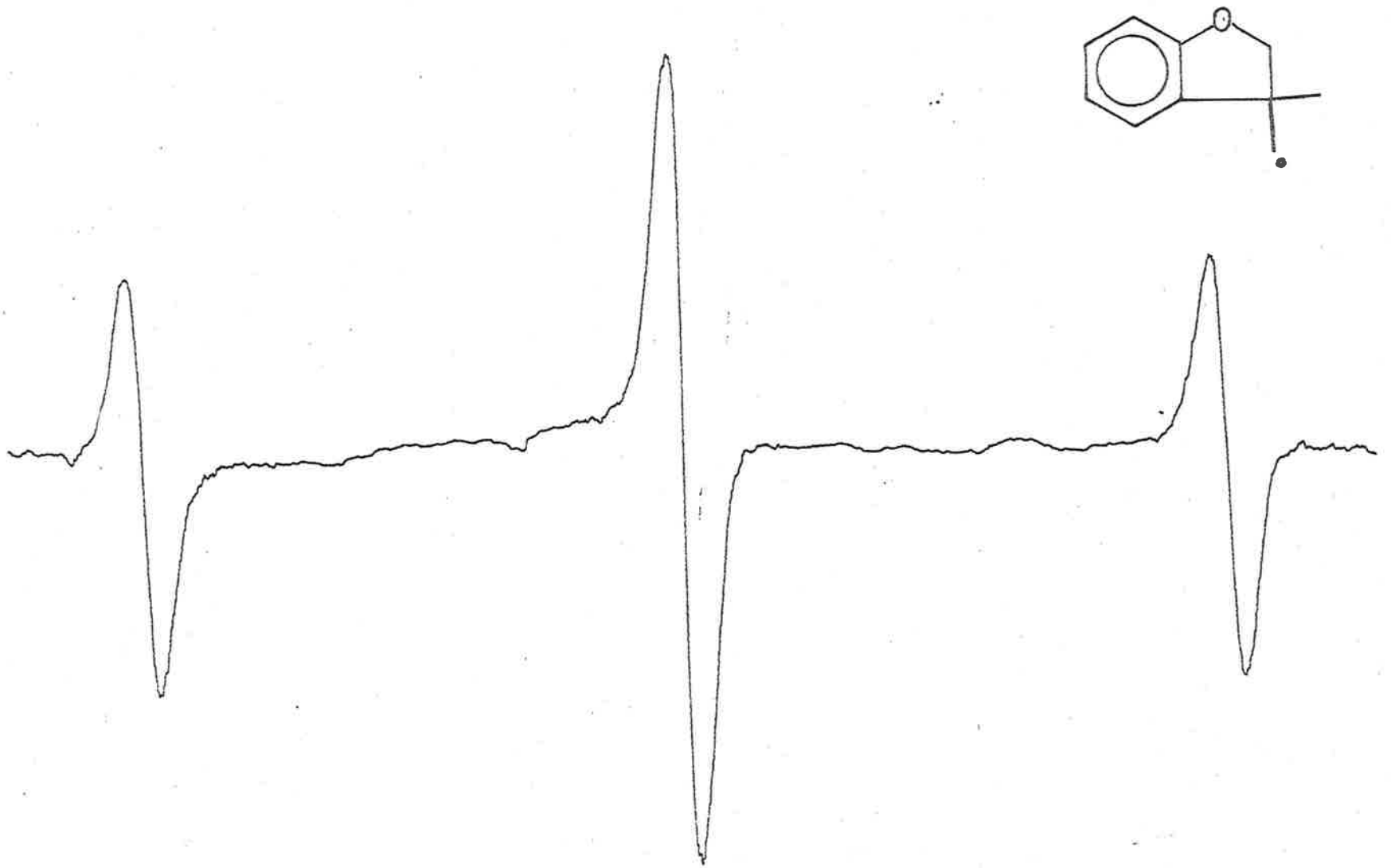


Figure 5.1.II

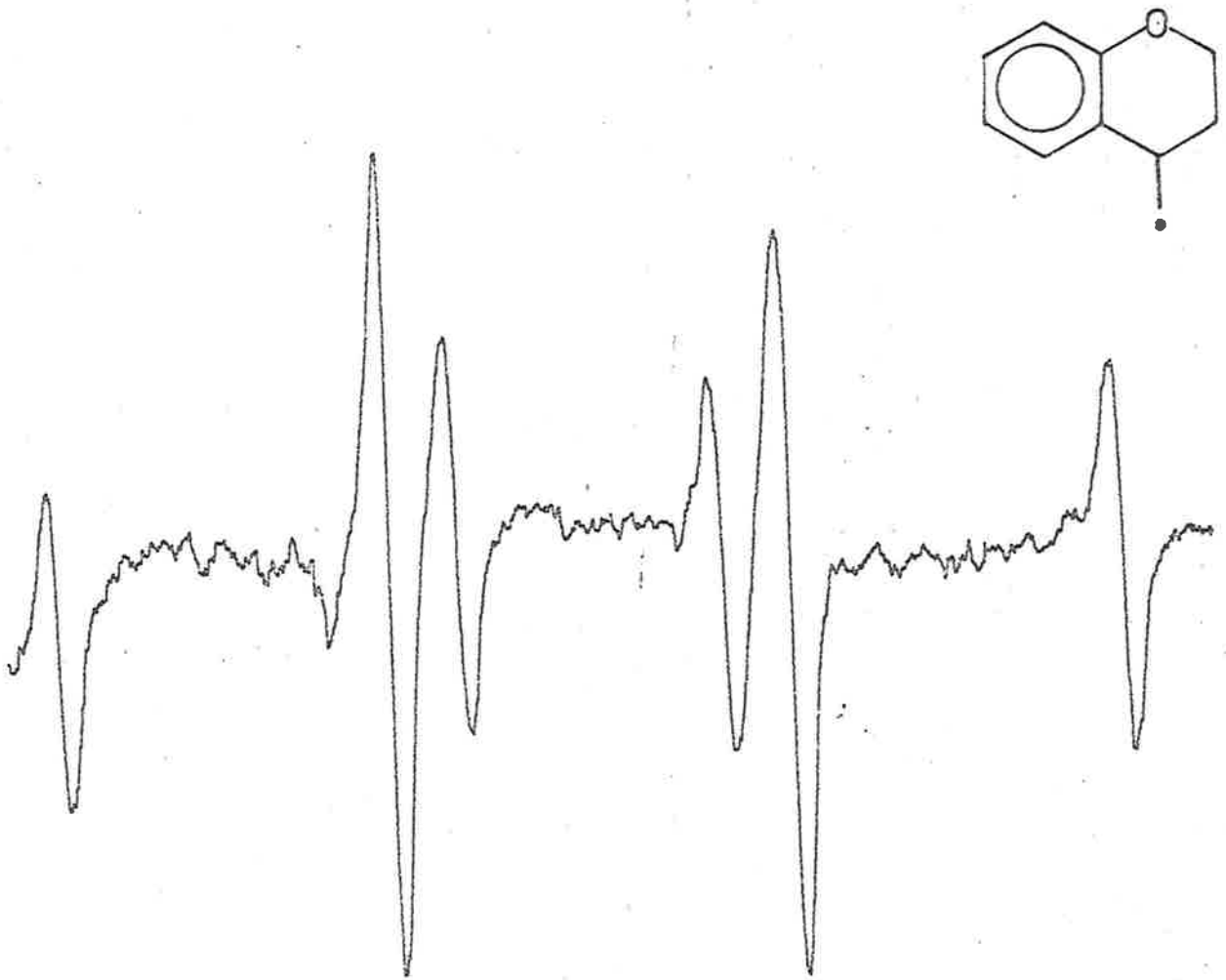
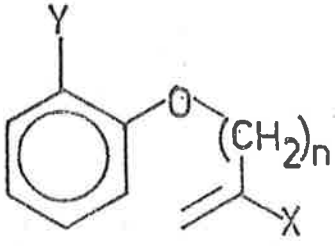
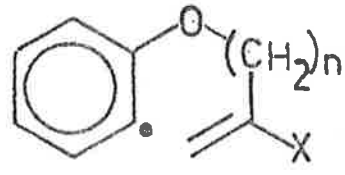


Figure 5.1.III



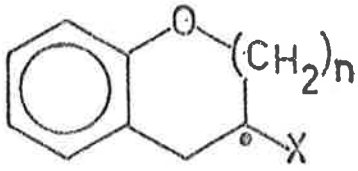
83

(a) n = 1, X = H, Y = N_2BF_4
(b) n = 1, X = CH_3, Y = N_2BF_4
(c) n = 2, X = H, Y = N_2BF_4
(d) n = 1, X = H, Y = NH_2
(e) n = 1, X = CH_3, Y = NH_2
(f) n = 2, X = H, Y = NH_2



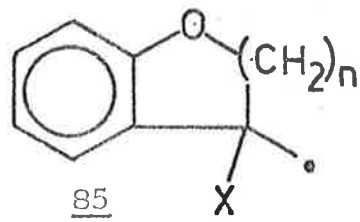
84

(a) n = 1, X = H
(b) n = 1, X = CH_3
(c) n = 2, X = H



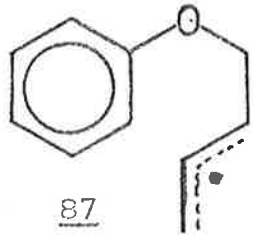
86

(a) n = 1, X = H
(b) n = 1, X = CH_3
(c) n = 2, X = H



85

(a) n = 1, X = H
(b) n = 1, X = CH_3
(c) n = 2, X = H



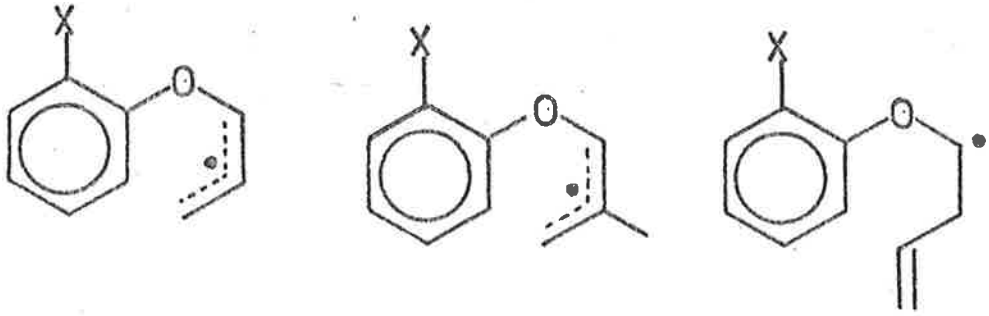
87

Scheme 5.1.I

Structures were assigned to the radical intermediates which gave rise to these spectra on the basis of their compatibility with the observed spectral characteristics. Moreover the spectra precluded the presence of other radical species which are listed in (i) to (v) with the respective multiplicities that may be predicted in brackets:-

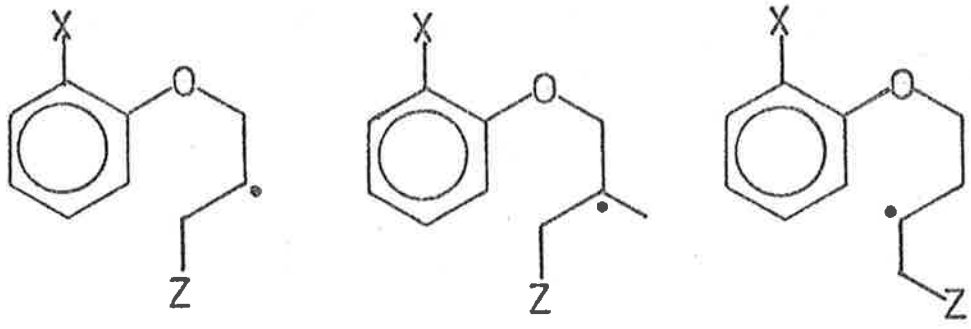
(i) Aryl radicals (86a), (86b) and (86c), (16 lines of considerable complexity[74] for each radical).

(ii) Radicals formed by intermolecular hydrogen-atom abstraction from the methylene groups next to the oxygen atoms i.e.:-



(12 lines,[81] 24 lines[81] and a triplet of doublets with a g-value of about 2.0031).

(iii) Radicals generated by intermolecular radical addition reactions, which would be expected to give the anti-Markownikoff adducts i.e.:-



(quintet of doublets, octet and quintet of doublets; possibly the spectra would be even more complex since the methylene groups next to the radical centre would probably be non equivalent).

(iv) Intramolecular radical addition reactions to the ends of the double bonds remote from the ring to give (86a), (86b) and (86c), (spectral characteristics of these adducts would be similar to the corresponding intermolecular adducts in (iii)).

(v) Intramolecular hydrogen-atom abstraction via a 6-membered transition state[74] in the radical (84c) to give the allylic radical (87), (36 lines of considerable complexity[81]).

Hence it was concluded that the cyclic radicals (85a), (85b) and (85c) gave rise to the spectra shown in Figures 5.1.I, 5.1.II and 5.1.III respectively. The low β-coupling constant in the spectrum of the radical (85a) may be attributed

to restricted rotation about the $C_\alpha - C_\beta$ bond due to non bonded interactions; the α-coupling constant is close to that of the free ethyl radical,[75] whereas the origin of the small γ-coupling is not clear. The α-coupling constant in the spectrum of radical (85b) is somewhat smaller than that expected for the free ethyl radical and the line widths are much broader than in the other two spectra. The inability to resolve γ-coupling is attributed to the increased number of γ-protons and to the restriction to rotation about the $C_\alpha - C_\beta$ bond due to the proximity of the methyl group to the radical centre. The α- and β-coupling constants in the spectrum of the radical (85c) were close to those of the free ethyl radical; γ-coupling was not observed in this case.

Beckwith and Norman[79] detected no e.p.r. absorption when the phenyl radical was generated in the presence of ethylene. This shows that intermolecular phenyl radical addition to an unactivated C=C double bond is much slower than the analogous intramolecular reactions.

An attempt was made to observe the e.p.r. spectrum of the o-methoxyphenyl radical, generated by reduction of o-methoxybenzenediazonium borofluoride. It was hoped that in the absence of competing intramolecular processes its

spectrum might be observed. However, no distinct spectrum could be discerned from the background signal which was probably due to stable polymeric radicals formed on the surface of the flow cell. On the other hand the fact that o-methoxyphenyl radicals were being formed was confirmed by addition to the reactant solutions of maleic acid and trimesic acid which produced spectra characteristic of the respective radical adducts[79]. Beckwith and Norman[79] have elaborated the reasons for the difficulties in recording the e.p.r. spectra of aryl radicals in solution.

It was stated previously that one of the requirements for the observation of the e.p.r. spectra of transient radical species is that they must be present in a certain minimum stationary concentration. This implies that the presence of radical intermediates in a reaction cannot be excluded on the grounds that their e.p.r. spectra are not observable. Hence for accurate studies of radical reactions, detailed product identification is necessary. The next section deals with such studies of products from the one-electron reduction of o-allyloxybenzenediazonium boro-fluoride (83a) with various reducing reagents.

5.2. EXPLORATORY PRODUCT STUDIES OF ARYL RADICAL CYCLIZATION REACTIONS

The effluent obtained after the measurement of the e.p.r. spectrum of the o-allyloxyphenyl radical, formed by the reduction of o-allyloxybenzenediazonium borofluoride (83a) with titanium (III) ethylenediaminetetraacetic acid at ~ pH 8, was extracted with ether; the ethereal layer was concentrated and subjected to short-path molecular distillation. Unfortunately only a very small amount of volatile product was obtained, thus showing that this method is not suitable for product analysis. In an attempt to increase the yield of monomeric products, several reducing agents were used for reduction of the above diazonium salt viz.:-

(i) A stirred two-phase system, with cyclohexane as the organic layer, using titanous ion as the reducing agent. It was hoped that the cyclohexane would act not only as a good hydrogen-atom donor but that it would also remove the products from the aqueous reaction phase thereby preventing further reaction of the products with radicals that are formed subsequently. Again volatile products were formed in a very low yield.

(ii) Two similar reductions with titanous chloride were carried out with ethanol present in the reaction mixture instead of cyclohexane. These

homogeneous reactions also failed to give good yields of monomeric products, in spite of the fact that ethanol is a good hydrogen-atom donor.

(iii) Chromous sulphate was also used as a reducing agent but again only tarry products were isolated.

(iv) Potassium ferrocyanide, a much milder reducing agent than titanous and chromous ions, was used to reduce the diazonium salt; the yield of volatile products was very low.

(v) The reduction procedure used for the observation of the e.p.r. spectrum was repeated, but this time the titanium (III) ethylenediaminetetraacetic acid complex was made up in a 1:1 methanol-water solution. Quantitative analysis by gas chromatography of the reaction products indicated that 3-methyl-2,3-dihydrobenzofuran and allyloxybenzene were formed in 11% and 2% yields respectively.

(vi) The reduction of the diazonium salt was also carried out by radicals derived from methoxide and isopropoxide ions[82] in methanol and isopropanol respectively; quantitative analysis by gas chromatography showed that the products contained 3-methyl-2,3-dihydrobenzofuran in 31% and 1.5% yield and allyloxybenzene in 4% and 7% yield

respectively. Chroman was not found amongst the products in either case.

The results obtained in (i) to (vi) deserve some comment. As it has been noted before a reasonably high concentration of radicals is necessary for the observation of their e.p.r. spectrum. In the reductions (i) to (v), which more or less duplicate the e.p.r. reduction conditions, one would expect a reasonably high concentration of radicals to be present at all times. This implies that competing radical processes such as dimerization and polymerization as well as disproportionation will lead to products other than allyloxybenzene and 3-methyl-2,3-dihydrobenzofuran. Aqueous hydrolysis of the diazonium salt will lead to phenolic by-products. It is therefore not surprising that the yields of the expected compounds were rather low in most cases. Disproportionation of the radical (85a) is also quite likely by interaction with the radical species present in the reductions[82] described in (vi).

It became obvious, therefore, that for detailed studies of the reactions of aryl radicals with olefinic ortho-substituents, a general method had to be developed which would give high yields of monomeric products.

The successful use of trialkylstannanes to generate alkyl

radicals for intramolecular rearrangement reactions has been dealt with in the introduction. These reagents provide high yields of reduced products, and furthermore permit estimation of the rates of such rearrangement reactions[55].

The use of trialkyl and triarylstannanes for the reduction of aryl bromides and iodides have been investigated by relatively few workers[54,83]. Moreover no positive proof for a free-radical chain mechanism, similar to that proven[55] for the reduction of alkyl halides, has been advanced for these reactions. Indeed Lorenz and his co-workers[83d] felt that a 4-centred mechanism best explained some of their experimental observations.

The ready accessibility of o-allyloxyiodobenzene allowed examination of its reduction with tri-n-butylstannane in benzene solution using azobisisobutyronitrile as the radical initiator. The reaction was clean and 3-methyl-2,3-dihydrobenzofuran was formed in quantitative yield. This result established the value of tributylstannane as a reagent for the study of intramolecular cyclization reactions of aryl radicals containing ortho-substituents with suitably disposed C=C double bonds.

It was shown by our e.p.r. studies that radical cyclization occurred when the double bond was in the 5-6 or 6-7 position relative to the radical centre. Alkyl radicals

containing double bonds in the 4-5 position relative to the radical centre fail to give cyclic products (see introduction). It was decided to examine the feasibility of such a cyclization reaction for aryl radicals. The reduction of o-vinyloxyiodobenzene with tributylstannane gave phenyl vinyl ether in almost quantitative yield; 2,3-dihydrobenzofuran the expected product from the intramolecular cyclization of the o-vinyloxyphenyl radical was not formed.

In the following chapter some of the synthetic work is described which was carried out to prepare suitable substrates and expected products in order to examine the nature of other aryl radical cyclization reactions.

5.3. SYNTHETIC WORK

(a) PREAMBLE

On the basis of the e.p.r. work and the exploratory product studies it was decided to prepare a number of iodobenzenes which are substituted in the ortho position with sidechains consisting of four or five atoms; in each case these sidechains contain a terminal C=C double bond.

For each aryl iodide* two possible cyclic products may be formed by radical attack at either end of the C=C double bond. These compounds and the open-chain nor-iodo compound* were synthesized by unambiguous routes.

In each case the open-chain nor-iodo compounds were prepared by a synthetic sequence which would be likely to be applicable for the synthesis of its ortho-iodo analogue. The reaction conditions were optimized before the preparation of the aryl iodides were undertaken.

All of the compounds that were synthesized were purified until analysis by gas chromatography indicated that impurities were present in less than 1%. Their structures were shown to be correct by physical techniques such as nuclear magnetic resonance spectroscopy, infrared spectroscopy and mass spectrometry. All new compounds gave satisfactory elemental analyses.

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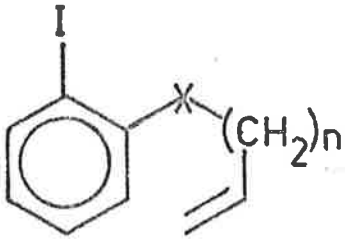
* The nomenclature used to identify these compounds is such as to correspond to the accepted nomenclature of the respective aryl radicals.

(b) SYNTHESES OF ARYL IODIDES AND THEIR POSSIBLE REDUCTION PRODUCTS

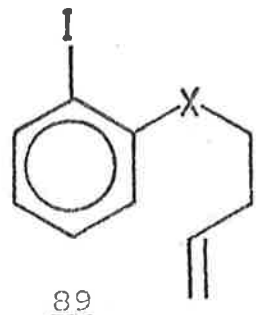
Comments will be made only on the syntheses of new compounds, or of compounds which were prepared by procedures which were different from those described in the literature.

For ease of reference, the aryl iodides prepared are shown in Scheme 5.3.I and their possible products by tributylstannane reduction in Scheme 5.3.II.



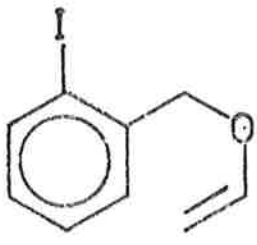
88

(a) X = O, n = 1
(b) X = NCH_3, n = 1
(c) X = CH_2, n = 1
(d) X = O, n = 0



89

(a) X = O
(b) X = NCH_3



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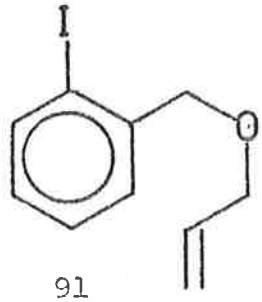

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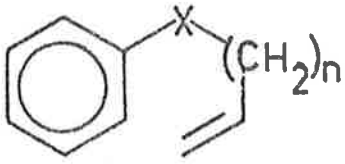
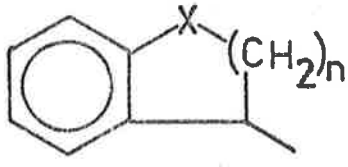
Scheme 5.3.I



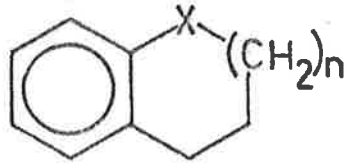
92

(a) X = O, n = 1
(b) X = O, n = 2
(c) X = NCH_3, n = 1
(d) X = NCH_3, n = 2
(e) X = CH_2, n = 1
(f) X = O, n = 0



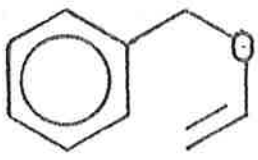
93

(a) X = O, n = 1
(b) X = O, n = 2
(c) X = NCH_3, n = 1
(d) X = NCH_3, n = 2
(e) X = CH_2, n = 1



94

(a) X = O, n = 1
(b) X = O, n = 2
(c) X = NCH_3, n = 1
(d) X = NCH_3, n = 2
(e) X = CH_2, n = 1
(f) X = O, n = 0



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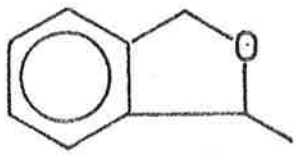

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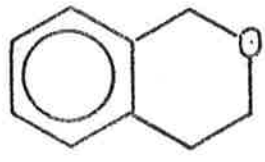

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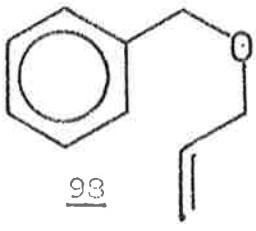

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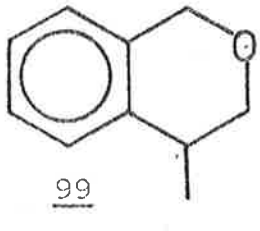

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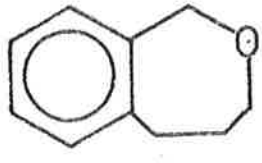


100

Scheme 5.3.II

o-Allyloxyiodobenzene (88a) was prepared by the alkylation of o-iodophenol with allyl bromide in acetone solution using potassium carbonate as the base. Chromatography on basic alumina removed the last traces of o-iodophenol from the product. 2,3-Dihydro-3-methylbenzofuran (93a) was obtained by the sodium-ethanol reduction[84] of 3-methylbenzofuran.

Alkylation of phenol with 4-bromo-1-butene in acetone solution using potassium carbonate as base gave only a very low yield of 3-butenyloxybenzene (92b). Similarly reactions of sodium phenoxide with 4-bromo-1-butene in dipolar aprotic solvents such as dimethyl formamide and dimethyl sulphoxide gave very low yields of the required ether (92b). It seemed possible that sodium phenoxide was acting as a base in the organic solvents used above causing the dehydrohalogenation of 4-bromo-1-butene to 1,3-butadiene. Silver phenoxide in boiling benzene was treated with 4-bromo-1-butene; in spite of the fact that similar alkylation reactions have been documented[85], none of the required ether (92b) was detected in the reaction mixture which was analysed periodically by gas chromatography. It has been noted[86] that 4-bromo-1-butene hydrolises very slowly to 4-hydroxy-1-butene in dilute aqueous base; it was found that the alkylation of sodium phenoxide with 4-bromo-1-butene in boiling water gave a workable yield of 3-butenyloxybenzene (92b). Similarly o-(3-butenyloxy)iodobenzene (89a) was

prepared from sodium o-iodophenolate and 4-bromo-1-butene. Both ethers were obtained in high purity after chromatography on basic alumina.

The preparations of o-(N-allyl-N-methylamino)iodobenzene (88b) and o-[N-(3-butenyl)-N-methylamino]iodobenzene (89b) proved somewhat difficult. Reactions of o-iodoaniline with less than a one molar equivalent of methyl iodide, allyl bromide and 4-bromo-1-butene respectively resulted in mixtures of mono- and di-N-alkylated products with the starting amine. Attempted separations of these mixtures by liquid chromatography and by fractional distillation were not successful. Alkylation of o-[N-(p-toluenesulphonyl)amino]iodobenzene with dimethyl sulphate in ethanolic sodium hydroxide solution gave o-[N-methyl-N-(p-toluenesulphonyl)amino]iodobenzene; hydrolysis of this tosylate in a mixture of acetic and hydrochloric acids left a purple residue in a very low yield. The reduction of amides with diborane has been shown[87] to give N-alkylamines in good yields. This procedure[87] was used to reduce o-(N-formylamino)iodobenzene. After several modifications in the reduction and in the work-up procedures o-(N-methylamino)iodobenzene was obtained in an excellent yield.

In all of the N-alkylation reactions moderate excesses of alkyl halides were used in order that the tertiary amine

products would be free of the starting materials, namely the respective secondary amines. Liquid chromatography on silica-gel was used to remove any quaternary salts which may have been formed. In this manner o-(N-allyl-N-methylamino)iodobenzene (88b) and o-[N-(3-butenyl)-N-methylamino]iodobenzene (89b) were obtained in good yields by alkylation of o-(N-methylamino)iodobenzene with allyl bromide and 4-bromo-1-butene respectively. The formation of (89b) was very slow: in order to complete the reaction it was necessary to add several molar equivalents of 4-bromo-1-butene over a period of 3 weeks. Alkylation of N-methylaminobenzene with 4-bromo-1-butene gave N-(3-butenyl)-N-methylaminobenzene (92d). The reductive formylation[88] of 4-methylquinoline gave 1-formyl-4-methyl-1,2,3,4-tetrahydroquinoline which, on reduction with lithium aluminium hydride, yielded 1,4-dimethyl-1,2,3,4-tetrahydroquinoline (93d). Lithium aluminium hydride reduction of homodihydrocarbostyril gave 2,3,4,5-tetrahydro-1-benzazepine (94, X=NH, n=2) which was methylated with methyl iodide to 1-methyl-2,3,4,5-tetrahydro-1-benzazepine (94d). Catalytic hydrogenation in ethanol-fluoroboric acid solution[89] of 1,3-dimethylindole gave 1,3-dimethylindoline (93c).

The synthesis of o-(vinyloxymethylene)iodobenzene (90) was effected by the mercuric acetate transvinylation reaction[90]

between o-iodobenzyl alcohol and ethyl vinyl ether. Reduction of o-acetyl benzoic acid gave ∝-methyl-o-xylene glycol, which was cyclodehydrated[92] to 1-methylphthalan (96).

Methods described in the literature for the preparation of allyloxymethylenebenzene (98) involve the addition of benzyl chloride or bromide to sodium allyloxide and usually (98) is obtained in moderate yields[93]. In view of the presence of excess base during the reaction, however, it was felt that such a method would not be suitable for the synthesis of the ortho-iodo analogue (91). Accordingly the addition procedure was reversed; sodium allyloxide was added to benzyl bromide to give (98) in high yield. Similarly the addition of sodium allyloxide to o-iodobenzyl bromide gave o-allyloxymethyleneiodobenzene (91) in good yield. Homoisochroman (100) was prepared from chloromethyl-(3-phenyl-n-propyl) ether by cyclodehydrohalogenation with anhydrous aluminium chloride[94]. Methylene chloride was used as the solvent for the reaction instead of carbon disulphide; this obviated the complicated work-up which is otherwise required[94].

o-(3-butenyl)iodobenzene (88c) was obtained by the addition of diiodoacetylene to the Grignard reagent prepared from o-(3-butenyl)chlorobenzene; this metal exchange

reaction[95] is forced to completion by the insolubility of the di-Grignard derivative of dichloroacetylene which is one of the species involved in the equilibrium. Earlier attempts at Grignard coupling between allylmagnesium bromide and o-iodobenzyl bromide resulted in a mixture of products.

Vinyloxybenzene (92f) was obtained from the p-toluene-sulphonate derivative of 2-phenoxyethanol by treatment with potassium t-butoxide in dimethylformamide solution. Dehydrohalogenation of o-(2-bromoethyloxy)iodobenzene using ethyldicyclohexylamine as base[96] gave impure o-vinyl-oxyiodobenzene (88d), which was purified by preparative gas chromatography.

(c) SYNTHESES OF AMINES FOR ELECTRON PARAMAGNETIC RESONANCE STUDIES

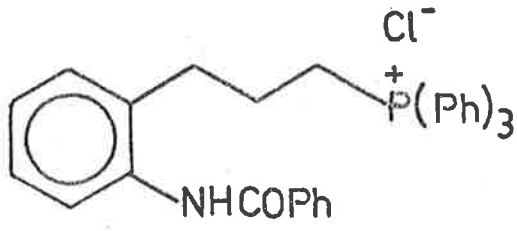
o-Allyloxyaniline (83d) was prepared by the alkylation of o-acetamidophenol with allyl bromide to give o-allyloxyacetanilide (83, n=1, X=H, Y=$COCH_3$) followed by hydrolysis[97]. This method was not entirely satisfactory since it did not give a pure product. The alternative route to (83d) involved alkylation of o-nitrophenol with allyl bromide to give o-allyloxynitrobenzene (83, n=1, X=H, Y=NO_2) which was reduced to the required amine (83d). Several reduction methods were investigated, including the use of an aqueous solution of sodium borohydride[98] and also a methanolic solution of hydrazine hydrate[99] with palladized charcoal as the catalyst in both instances; yields from these reductions were not satisfactory. The reductions of o-allyloxynitrobenzene with stannous chloride dihydrate[100] in concentrated hydrochloric acid-ethanol solution gave an excellent yield of pure o-allyloxyaniline (83d) after one distillation. The reaction of o-nitrophenol with 2-methylallyl chloride in boiling acetone in the presence of potassium carbonate and sodium bromide gave o-(2-methylallyloxy)nitrobenzene (83, n=1, X=CH_3, Y=NO_2) which was reduced with stannous chloride[100] to o-(2-methylallyloxy)aniline (83e) in a good yield. The alkylation of o-nitrophenol with 4-bromo-1-butene gave o-(3-butenyloxy)nitrobenzene (83, n=2, X=H, Y=NO_2); which on

reduction with stannous chloride[100] yielded o-(3-butenyloxy)-aniline (83f).

Several reaction schemes were devised for the unambiguous synthesis of o-(3-butenyl)aniline (104). The first involved the preparation of the triphenylphosphonium salt (102) from o-(3-chloropropyl)benzanilide (101), followed by treatment of (102) with sodium hydride and formaldehyde gas to give (103). Hydrolysis of (103) would have yielded the required amine (104). Treatment of the phosphonium salt (102) with sodium hydride, however, produced no ylide. (Scheme 5.3.III) It was felt that the amide proton of (103) may be acidic enough to be removed by sodium hydride, hence it was thought that the phthalimide analogue of (101) would be a more convenient intermediate in the synthetic sequence. Treatment of the phthalamic acid derivative of tetrahydroquinoline (105, X=H) with phosphorous pentachloride[101] or thionyl chloride[102] under many different reaction conditions did not give any of the required phthalimide (106) but instead formed the acid chloride (105, X=Cl).

Treatment of o-nitrotoluene with potassium ethoxide and diethyl oxalate has been shown[103] to give ethyl (o-nitrophenyl)pyruvate by alkylation on the methyl group. Accordingly it was felt that o-nitrotoluene might be alkylated in the same manner with allyl bromide and also with 4-bromo-

101



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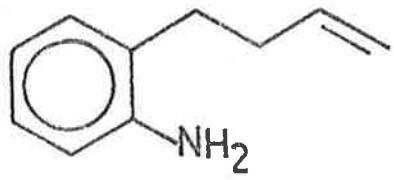

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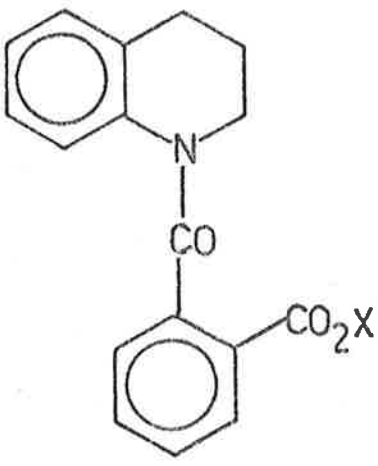

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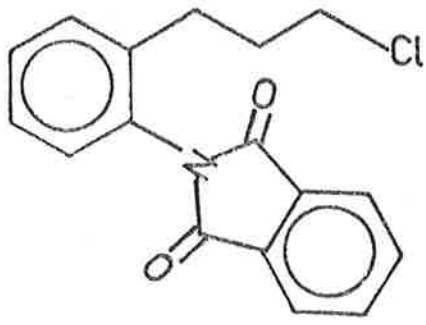


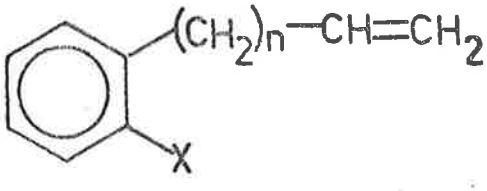
106

Scheme 5.3.III

1-butene in the presence of a non-nucleophilic base such as sodium hydride; at room temperature none of the required products were formed, and at higher temperatures the reactions became violent leading to the formation of tarry products.

The Fittig-Tollens coupling[104] of o-nitrobromobenzene with 4-bromo-1-butene gave a number of by-products and a very low yield of the required o-(3-butenyl)nitrobenzene.

The alkylation of toluic acid with bromobutane using lithium diisopropylamide as base was mentioned recently in a note by Creger[105]. By alkylation[105] of toluic acid with allyl bromide and 4-bromo-1-butene we prepared o-(3-butenyl)-benzoic acid (107a) and o-(4-pentenyl)benzoic acid (107b) respectively; unfortunately both products contained some toluic acid which could not be removed by crystallization.



107 (a) n=2, X=CO_2H

(b) n=3, X=CO_2H

(c) n=2, X=COCl

(d) n=2, X=$CONH_2$

(e) n=2, X=NH_2

The mixture of o-(3-butenyl)benzoic acid (107a) and toluic acid was treated with oxalyl chloride to give (107c) and o-toluyl chloride, which were converted with aqueous ammonium hydroxide solution to (107d) and o-toluamide; this mixture of amides was treated with sodium hypochlorite solution to give, by the Hofmann rearrangement, o-(3-butenyl)aniline (107e) and o-toluidine. The yield of (107e) was insufficient for the proposed e.p.r. studies.

5.4. ARYL RADICAL CYCLIZATION REACTIONS BY THE REDUCTION OF ARYL IODIDES WITH TRIBUTYLSTANNANE

To facilitate comparison between different systems the reductions described below were carried out under the following standard conditions:-

(a) The reactions were all of 24 hours duration.

(b) The reaction mixtures in benzene solution were sealed under vacuum into reaction tubes of the same size.

(c) Reaction temperatures were 130 ± 3°.

(d) Azobisisobutyronitrile was used as the radical initiator in each case.

(e) The initial concentration of the aryl iodide was approximately the same in each case.

(f) Each aryl iodide was reduced using four different concentrations of tributylstannane, which were 1,2,4 and 8 molar equivalents with respect to the iodo compound.

(g) All reductions were carried out in duplicate.

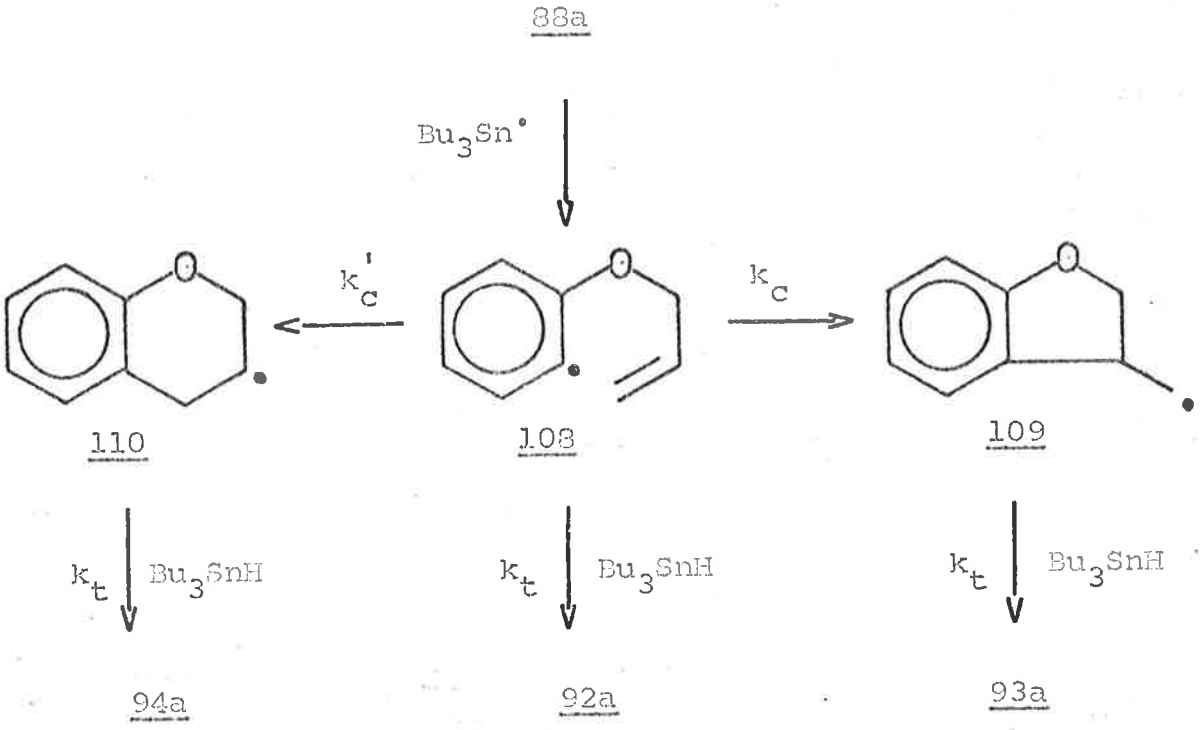
(h) Blanks consisting of the aryl iodide and azobisisobutyronitrile in benzene solution were run concurrently with the reduction mixtures; this ascertained that the iodo compound did not rearrange under the reaction conditions.

Details of the methods used are given in the experimental

section. It suffices to say here that the reaction mixtures were quenched with accurately weighed aliquots of carbon tetrachloride containing a known amount of internal standard. The mixtures were then analysed by gas chromatography; the area under each peak in the chromatogram was determined with the aid of a printing integrator. Absolute yields were calculated by means of calibration graphs obtained by analysing, under identical conditions, accurately prepared mixtures of the internal standard and the expected products.

Tables 5.4.I to 5.4.VIII show the results obtained in the reductions. Schemes 5.4.I to 5.4.VIII illustrate the reactions which might be expected to take place in each case.

(i) Reduction of o-allyloxyiodobenzene (88a)

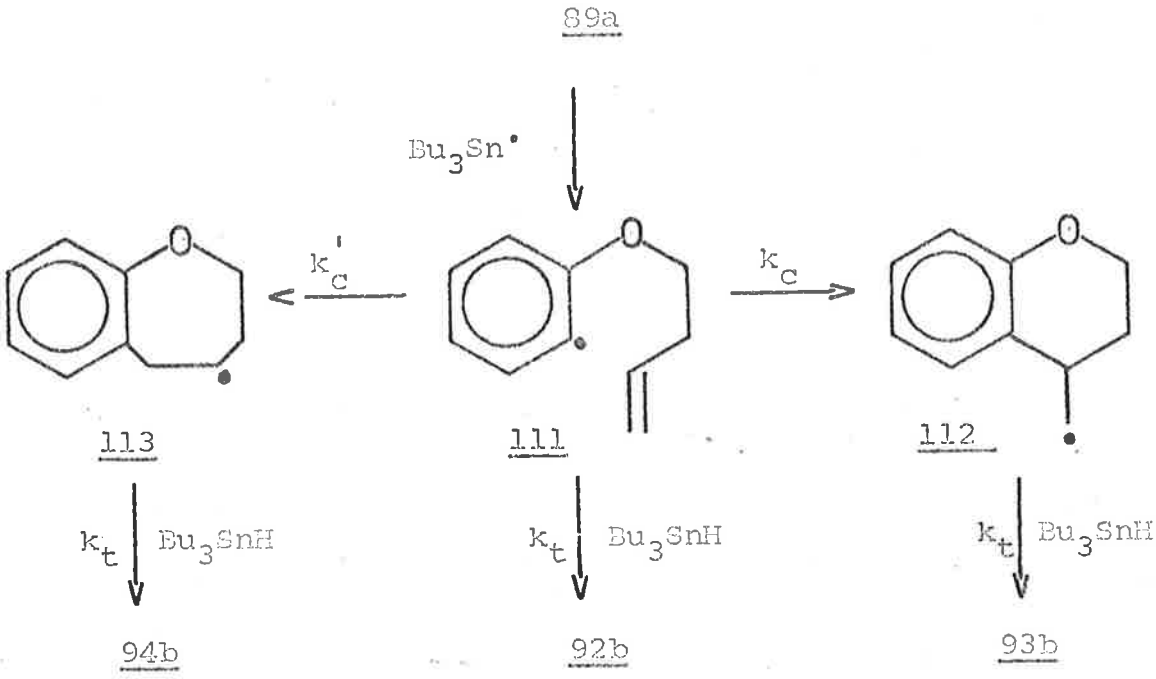


Scheme 5.4.I

Initial concn. of 88a (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92a (%)	Relative yield of 93a (%)	Relative yield of 94a (%)	Absolute yield of reduction (%)
0.086	0.086	0	100	0	72
0.086	0.172	trace	100	0	quant.
0.086	0.344	trace	100	0	quant.
0.086	0.688	trace	100	0	quant.

Table 5.4.I

(ii) Reduction of o-(3-butenyloxy)iodobenzene (89a)

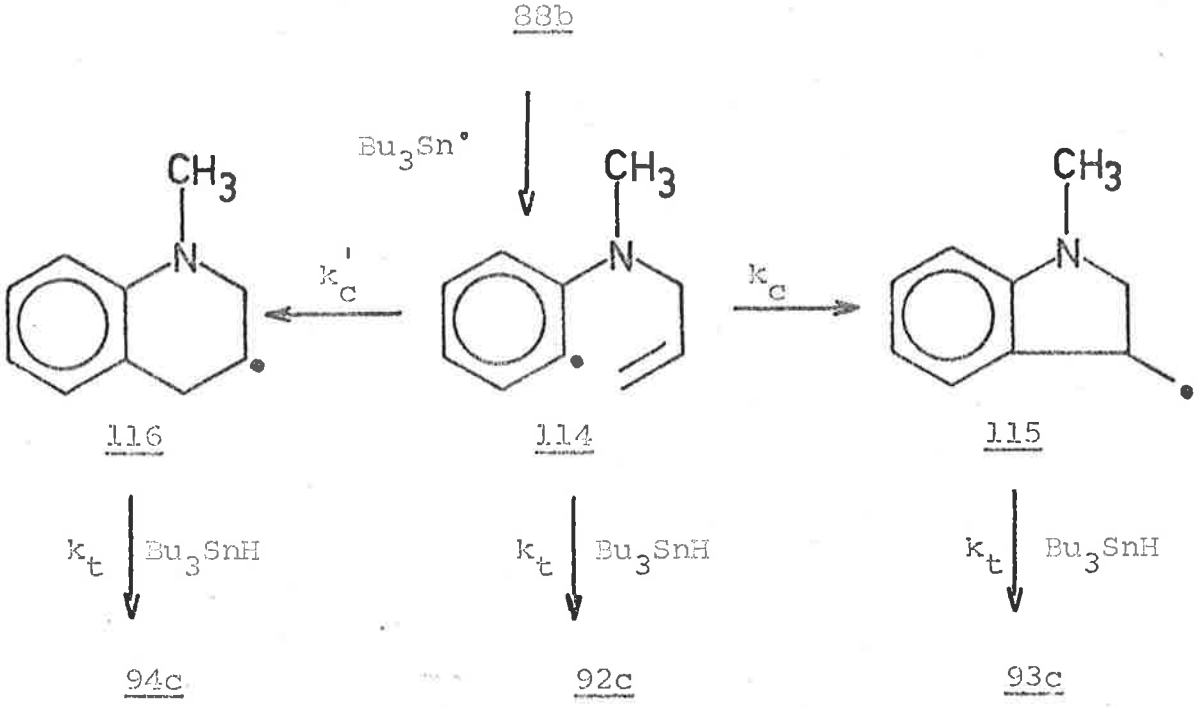


Scheme 5.4.II

Initial concn. of 89a (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92b (%)	Relative yield of 93b (%)	Relative yield of 94b (%)	Absolute yield of reduction (%)
0.082	0.074	14	86	0	52
0.082	0.150	19	81	0	87
0.082	0.299	25	75	0	96
0.082	0.596	38	62	0	99

Table 5.4.II

(iii) Reduction of o-(N-allyl-N-methylamino)iodobenzene (88b)

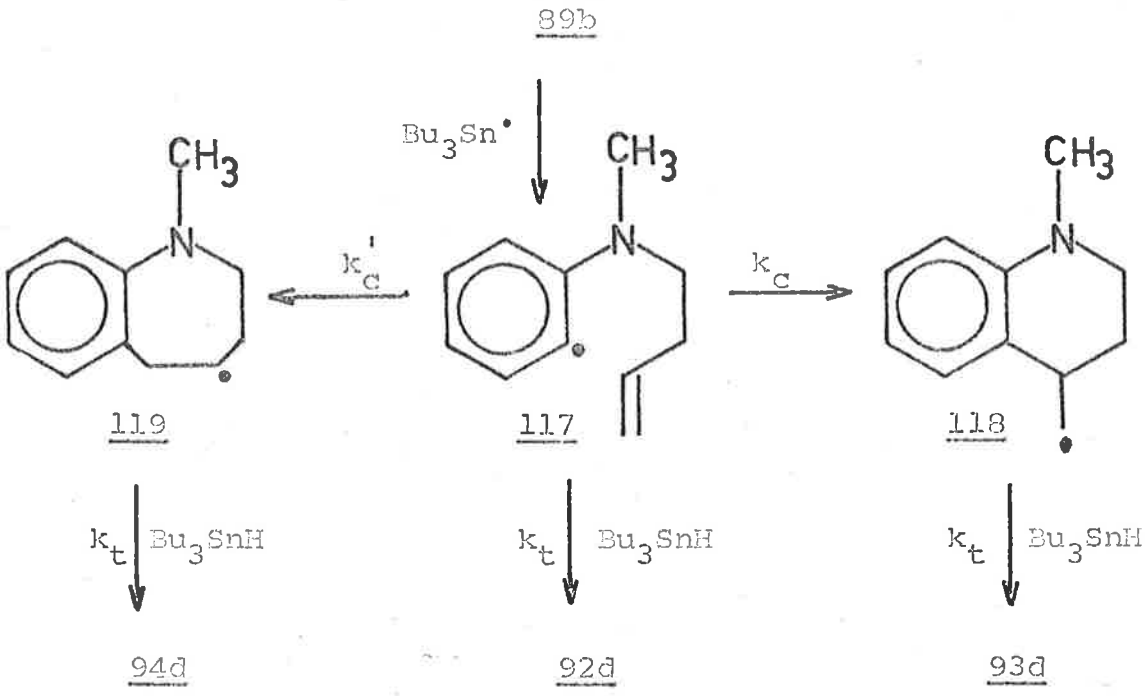


Scheme 5.4.III

Initial concn. of 88b (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92c (%)	Relative yield of 93c (%)	Relative yield of 94c (%)	Absolute yield of reduction (%)
0.073	0.069	4	96	0	82
0.074	0.146	7	93	0	96
0.074	0.294	11	89	0	93
0.074	0.592	15	85	0	88

Table 5.4.III

(iv) Reduction of o-[N-(3-butenyl)-N-methylamino]iodobenzene (89b)



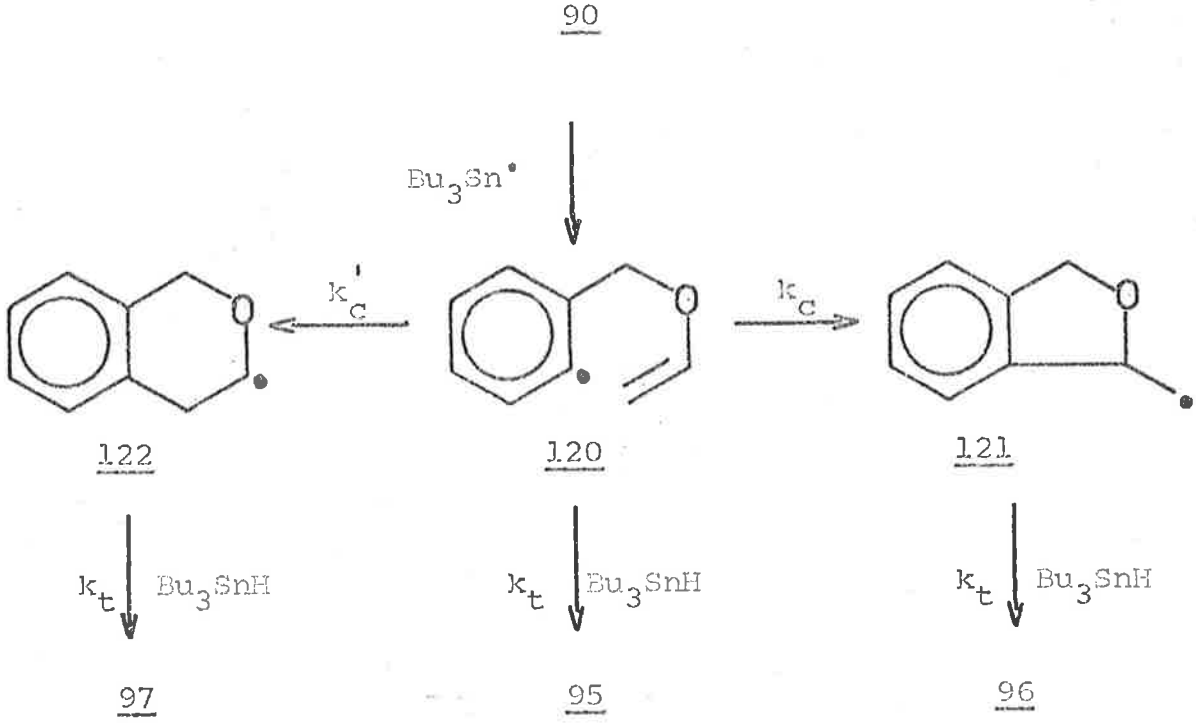
Scheme 5.4.IV

Initial concn. of 89b (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92d* (%)	Relative yield of 93d (%)	Relative yield of 94d (%)	Absolute yield of reduction (%)
0.073	0.074	36	64	0	55
0.073	0.148	38	62	0	93
0.073	0.300	43	57	0	86
0.073	0.600	48	52	0	87

*see later

Table 5.4.IV

(v) Reduction of o-vinyloxymethyleneiodobenzene (90)

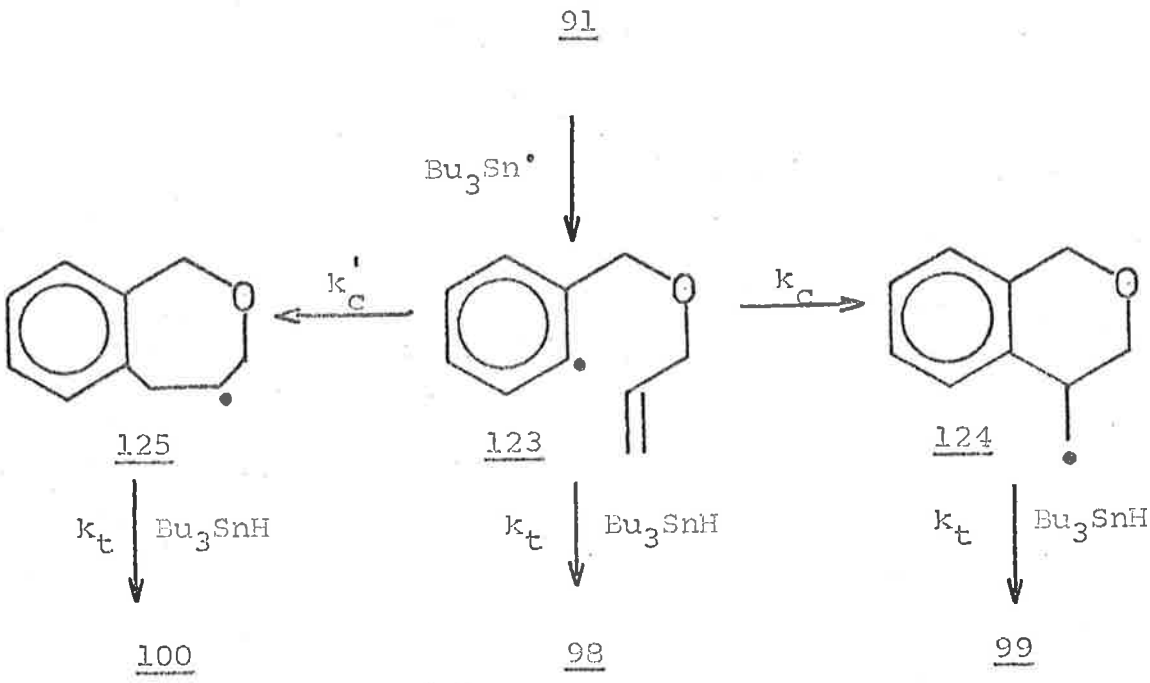


Scheme 5.4.V

Initial concn. of 90 (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 95 (%)	Relative yield of 96 (%)	Relative yield of 97 (%)	Absolute yield of reduction (%)
0.073	0.067	23	77	trace	37
0.073	0.155	36	64	trace	77
0.073	0.316	55	45	trace	99
0.073	0.612	76	24	trace	98

Table 5.4.V

(vi) Reduction* of o-allyloxymethyleneiodobenzene (91)



Scheme 5.4.VI

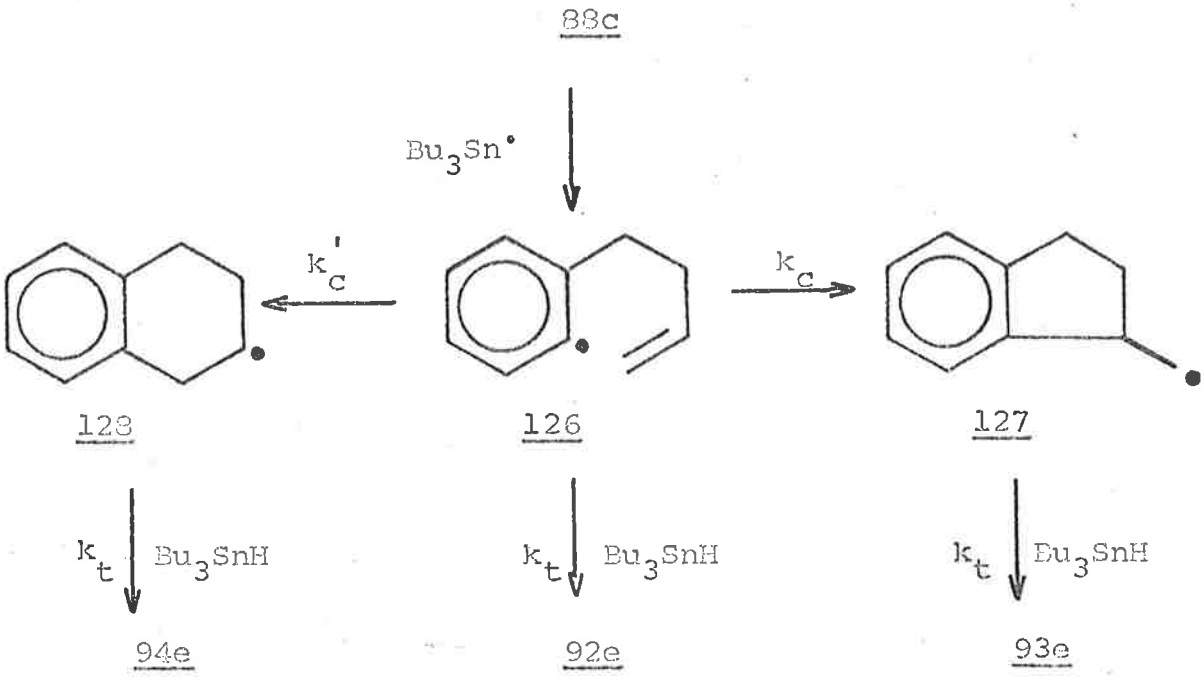
Initial concn. of 91 (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 98** (%)	Relative yield of 99 (%)	Relative yield of 100 (%)	Absolute yield of reduction (%)
0.072	0.077	57	43	0	13
0.072	0.148	66	34	0	20
0.072	0.300	76	24	0	68
0.072	0.599	83	17	0	85

Table 5.4.VI

* Reaction time 12 hours
(Unreacted iodo compound (91) was present in all the reaction mixtures)

** see later

(vii) Reduction of o-(3-butenyl)iodobenzene (88c)

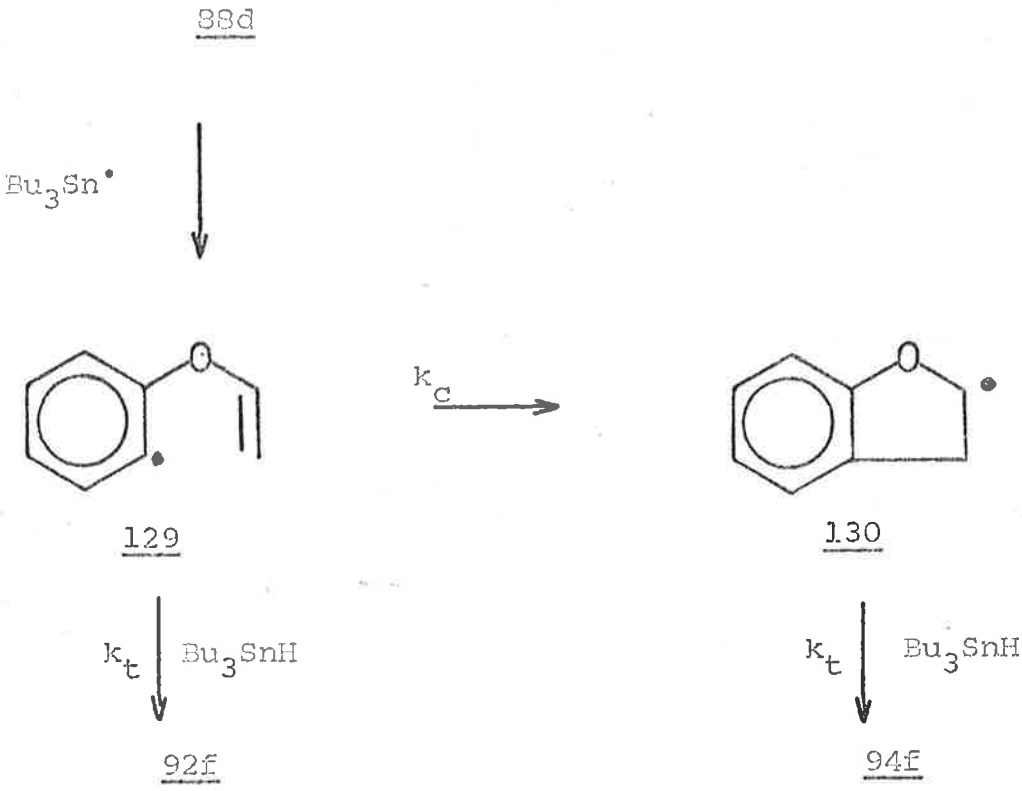


Scheme 5.4.VII

Initial concn. of 88c (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92e (%)	Relative yield of 93e (%)	Relative yield of 94e (%)	Absolute yield of reduction (%)
0.073	0.067	10	90	trace	63
0.074	0.138	17	83	trace	97
0.074	0.289	38	62	trace	quant.
0.073	0.563	50	50	trace	quant.

Table 5.4.VII

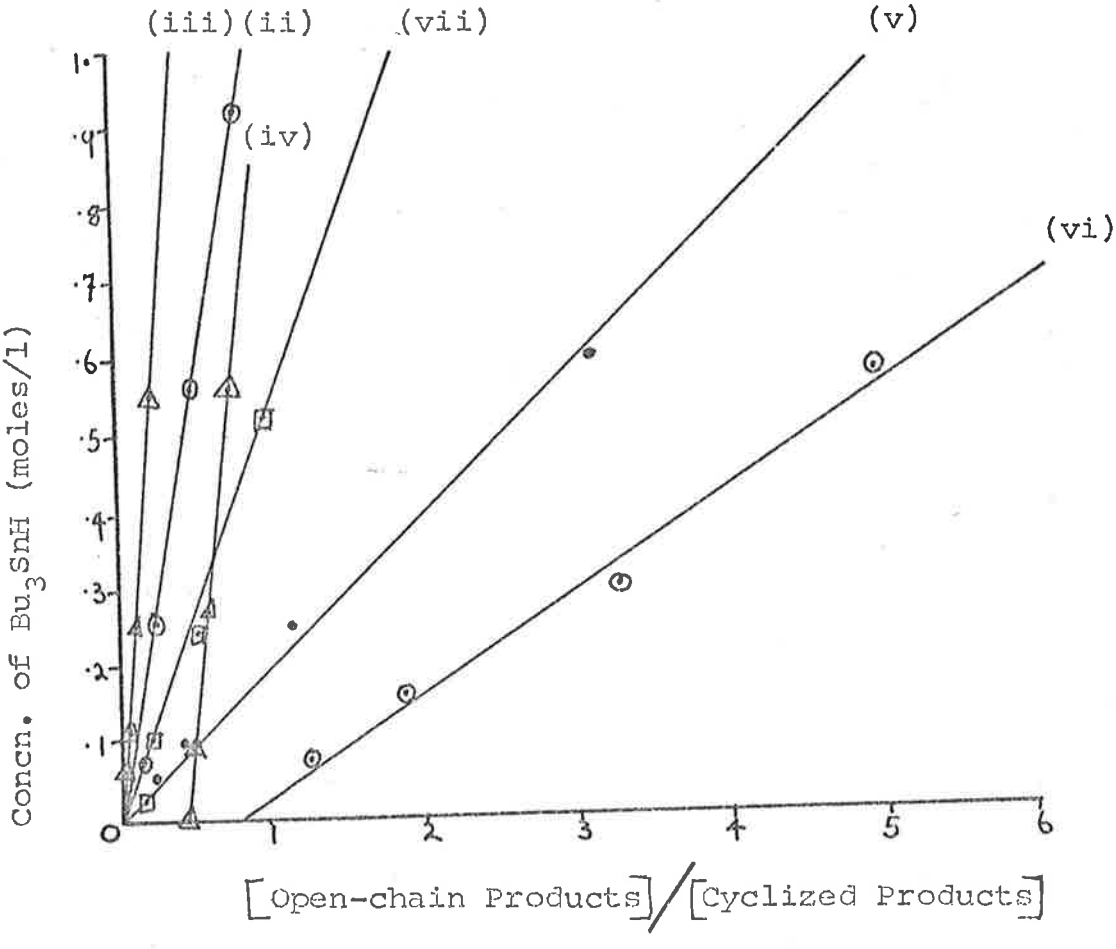
(viii) Reduction of o-vinyloxyiodobenzene (88d)



Scheme 5.4.VIII

Initial concn. of 88d (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92f (%)	Relative yield of 94f (%)	Absolute yield of reduction (%)
0.092	0.166	100	0	92
0.100	0.830	100	0	94

Table 5.4.VIII



Key:- The numbers (ii) to (vii) correspond to the numbering of the reductions listed above.

Diagram 5.4.I

For each individual reduction listed in Tables 5.4.I to 5.4.VII the average concentration of stannane during the reaction was calculated; e.g.:-

(a) initial concentration of iodo compound = 0.073 moles/l.

(b) initial concentration of tributylstannane = 0.067 moles/l.

(c) absolute yield of reduction = 63%.

(d) hence average concentration of stannane =

$$\frac{0.067 + (0.067 - (0.073 \times 0.63))}{2} \text{ moles/l}$$

= 0.044 moles/l.

The straight lines numbered (ii) to (vii) in Diagram 5.4.I were obtained by plotting against the average stannane concentration the ratio of the relative yield of the uncyclized product to the relative yield of the cyclized product for each individual reduction listed in Tables 5.4.II to 5.4.VII.

Normally, with slower cyclization reactions in which the average stannane concentrations are lower than the ones employed here, the ratios of the relative yields of cyclized products to the relative yields of uncyclized products are plotted against the reciprocal of the average stannane concentrations[55,58]. From such plots the ratio of the rate

constant of cyclization (k_c) to the rate constant of hydrogen-atom transfer with the stannane (k_t) are calculated from the following equation[55,58]:-

$$\frac{[\text{cyclized products}]}{[\text{open chain product}]} = \frac{k_c}{k_t} \times \frac{1}{[Bu_3SnH]}$$

For convenience this equation may be used in its reciprocal form i.e.:-

$$\frac{[\text{open chain product}]}{[\text{cyclized products}]} = \frac{k_t}{k_c} \times \frac{[Bu_3SnH]}{1}$$

The reciprocal form of the equation was found to be more suitable for our results since at low stannane concentrations $[\text{open chain product}] / [\text{cyclized products}]$ converges to zero because the relative yields of cyclized products are much larger than those of the open chain products.

Table 5.4.IX shows the values of k_c/k_t obtained from the plots (ii) to (vii), in Diagram 5.4.I, with the aid of the latter equation.

The values of k_c are based on the assumption that k_t for aryl radicals has the value of $1 \times 10^6 M^{-1} sec^{-1}$ as determined for alkyl radicals[55]. It is likely, however, that k_t for aryl radicals has a somewhat higher value for alkyl radicals.

Radical	108	111	114	117	120	123	126
k_c/k_t (M)	63	0.93	3.1	*	0.17	*	0.54
k_c (sec^{-1})	$6.3x10^7$	$9.3x10^5$	$3.1x10^6$	*	$1.7x10^5$	*	$5.4x10^5$

*see later

Table 5.4.IX

This statement is based on the following rationale:-

(a) It has been shown that for alkyl radicals the value of k_t increases in the order:-

t-butyl < n-hexyl ≤ cyclohexyl < methyl

The above order is approximately the same as the order of the strengths of the C-H bonds which are formed by the hydrogen-atom transfer process.

(b) The strength of the C-H bond formed in the reaction of an aryl radical with tributylstannane is higher than that of any of the C-H bonds referred to in (a).

(c) Hence if the relationship between the strength of the C-H bond formed and the value of k_t, as shown in (a), is general, then k_t might be expected to have higher values for aryl radicals than for alkyl radicals. This rationalization does not

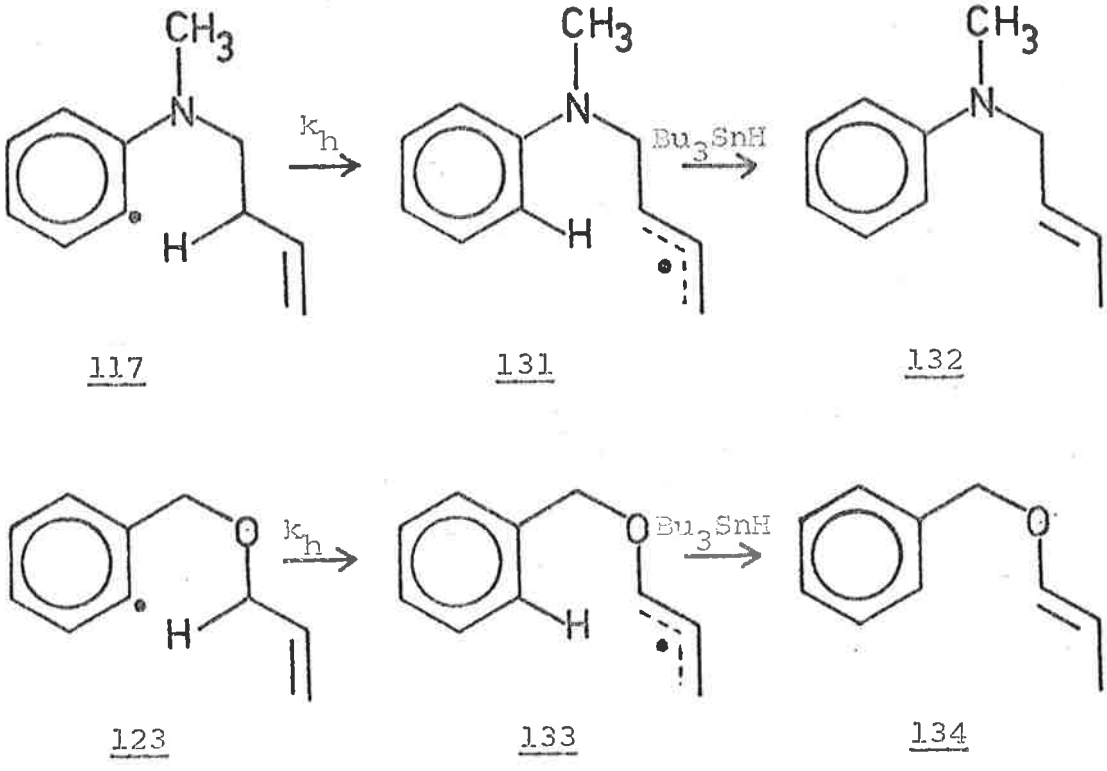
take into account any steric factors which might hinder the approach of a tributylstannane towards the radical centre.

The foregoing discussion implies that in fact the values of k_t for aryl radicals are higher than the average value of $10^6 M^{-1} sec^{-1}$ calculated for alkyl radicals. The values of k_c in Table 5.4.IX may therefore be taken as the lowest limits rather than the actual values of k_c. Nevertheless this error in k_t is likely to be constant throughout the series of aryl radicals, so that the relative values of k_c would still be the same.

The actual value of k_c/k_t for the reduction of o-allyloxyiodobenzene (88a) could not be obtained accurately since even when the average concentration of stannane was about 0.64 moles/l, the relative yield of allyl phenyl ether was less than 1%. This places a lower limiting value on k_c/k_t of about 63 M; thus a lower limiting value of 6.3×10^7 sec^{-1} on k_c for the cyclization of the o-allyloxyphenyl radical (108).

Two of the straight lines (iv) and (vi) in Diagram 5.4.I do not pass through the origin. This indicates that in the two reactions, from which plots (iv) and (vi) are derived, apart from the usual radical cyclization reaction and the intermolecular hydrogen-atom transfer there is an alternative competing process operating. As can be seen

in Scheme 5.4.IX radicals (117) and (123) are both suitably constituted for intramolecular hydrogen-atom transfer reactions via 6-membered transition states[74] to give the allylic radicals (131) and (133) respectively.



117 131 132

123 133 134

Scheme 5.4.IX

Gas chromatographic analysis of the products of the reductions in question supports such intramolecular hydrogen-atom transfer processes in the following manner:-

(a) Amongst the reaction products of o-[N-(3-butenyl)-N-methylamino]iodobenzene (89b), there was a peak eluted closely before that due to the uncyclized reduced product (92d) and which could not be resolved from it completely; this peak

probably represents the compound (132) formed by hydrogen-atom abstraction from the stannane by the allylic radical (131) at its terminal carbon atom.

(b) Similarly amongst the reduction products of o-allyloxymethyleneiodobenzene (91) there was also an unresolved peak next to that due to (98) which probably represents (134) formed in a similar manner to (132).

It must be mentioned, however, that the trans-stereochemistry assigned to (132) and to (134) are only based on the assumption that these are more likely to be formed than the cis-isomers; it is probable however that products (132) and (134) are in fact mixtures of cis- and trans-isomers.

Such a competing intramolecular hydrogen-atom transfer was absent in the reactions of the o-(3-butenyloxy)phenyl radical (111) even though a similar 6-membered transition state cannot be excluded on inspection of its molecular model.

Returning now to the case of the two straight lines (iv) and (vi) which did not pass through the origin. It was observed that the intercepts of these lines corresponding to zero stannane concentration had the values of 0.55 and 0.90 respectively. These intercepts may be interpreted in terms of the following treatment which may be applied to the

kinetics of the competing processes involved in either of these reductions:-

$$\frac{dA}{dt} = k_t [X] [Bu_3SnH]$$

$$\frac{dB}{dt} = k_c [X]$$

$$\frac{dC}{dt} = k_h [X]$$

thus $$\frac{\frac{dA}{dt} + \frac{dC}{dt}}{\frac{dB}{dt}} = \frac{k_t [X] [Bu_3SnH] + k_h [X]}{k_c [X]}$$

$$= \frac{k_t [Bu_3SnH] + k_h}{k_c}$$

hence $$\frac{[A] + [C]}{[B]} = \frac{k_t [Bu_3SnH]}{k_c} + \frac{k_h}{k_c}$$

when $[Bu_3SnH] = 0$ then $[A] = 0$

therefore $$\frac{[C]}{[B]} = \frac{k_h}{k_c}$$

Key:- k_t = rate constant of hydrogen-atom transfer of aryl radicals (X) with the stannane to give open-chain products (A).

k_c = rate constant of cyclization of the aryl

radicals (X) to the cyclic radicals (B).

k_h = rate constant of the intramolecular hydrogen-atom transfer in the aryl radicals (X) to form the allylic radicals (C).

Thus it can be seen that the value of the intercept of the straight line (iv) (Diagram 5.4.I) at zero stannane concentration represents the ratio of the rate constant of intramolecular hydrogen-atom transfer (k_h) to the rate constant of intramolecular cyclization (k_c). A similar argument applies to the intercept of line (vi) at zero stannane concentration. These intercepts correspond to the ratios of the relative yields of open-chain products formed by intramolecular hydrogen-atom transfer to the relative yields of the products formed by radical cyclization at any one stannane concentration since the two rate constants involved in these processes are independent of the stannane concentration. This now allows us to calculate what proportion of the open-chain reduced products were formed by the intramolecular process and therefore what fraction was formed by intermolecular hydrogen-atom transfer with the stannane e.g. in Table VI:-

(a) Relative yield of cyclic product (99) = 43%

(b) Relative (combined) yield of open-chain reduced products = 57%

(c) The value of the intercept at zero stannane

concentration = 0.90

(d) By the above treatment the relative yield of open-chain product by intramolecular hydrogen-atom abstraction = 43 x 0.90 = 38.7%

(e) By subtraction, the relative yield of open-chain product (98) formed by intermolecular hydrogen-atom transfer with the stannane = (57 - 38.7) = 18.3%

On this basis the Tables 5.4.IV and 5.4.VI may be presented in the modified form of Tables 5.4.IV* and 5.4.VI* respectively:-

Initial concn. of 89b (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92d by k_t (%)	Relative yield of 92d+132 by k_h (%)	Relative yield of 94d by k_c (%)	Absolute yield of reduction (%)
0.073	0.074	0.8	35.2	64	55
0.073	0.148	3.9	34.1	62	93
0.073	0.300	11.65	31.35	57	86
0.073	0.600	19.4	28.6	52	87

Table 5.4.IV*

Initial concn. of 91 (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 98 by k_t (%)	Relative yield of 98+134 by k_h (%)	Relative yield of 99 by k_c (%)	Absolute yield of reduction (%)
0.072	0.077	18.3	38.7	43	13
0.072	0.148	35.4	30.6	34	20
0.072	0.300	54.4	21.6	27	68
0.072	0.599	67.7	15.3	17	85

Table 5.4.VI*

It is now possible with the figures available in Tables 5.4.IV* and 5.4.VI* to plot against the average stannane concentration the ratios of the relative yields of open-chain products (formed by intermolecular hydrogen-atom abstraction from the stannane) to the relative yields of cyclic products. This gives the line (iv*) from the figures in Table 5.4.IV*, and the line (vi*) from the figures in Table 5.4.VI*. Diagram 5.4.II shows these lines, both of which pass through the origin. The respective values of k_c/k_t, which may now be calculated as for the other reductions, are 1.5 M and 0.15 M for the reductions of o-[N-(3-butenyl)-N-methylamino]-iodobenzene (89b) and o-(allyloxymethylene)iodobenzene (91) respectively.

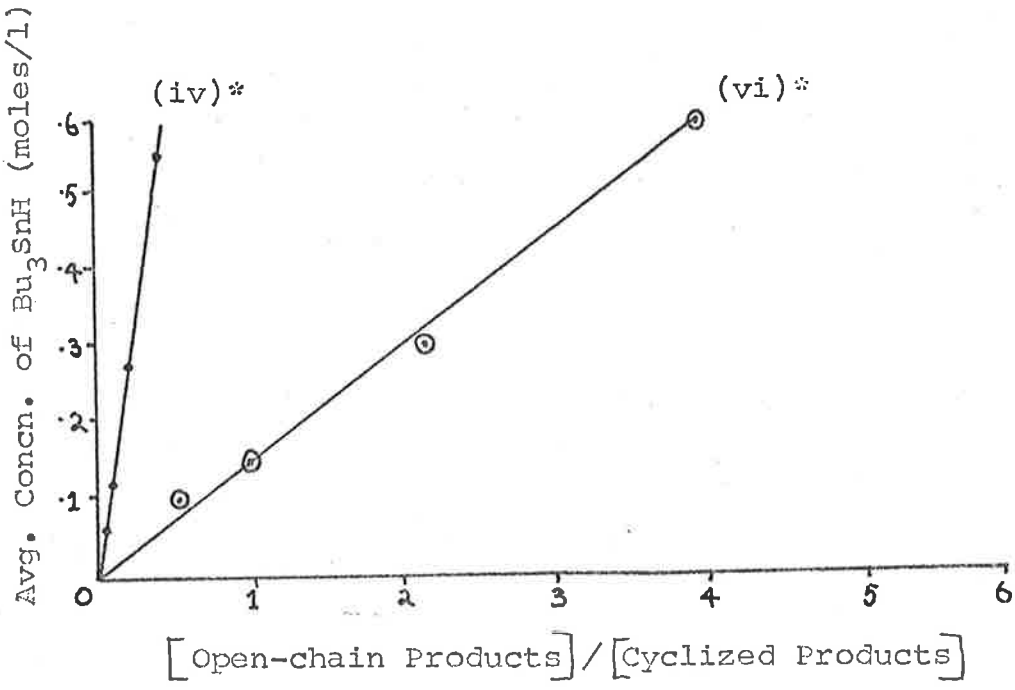


Diagram 5.4.II

Taking the value of k_t to be $1 \times 10^6 M^{-1}sec^{-1}$, the respective values of k_c are therefore $1.5 \times 10^6 sec^{-1}$ and $1.5 \times 10^5 sec^{-1}$.

It was shown above that the ratios of k_h to k_c are 0.55 and 0.90 respectively for these abovementioned reductions. This allows us now to deduce the values of the rate constants of intramolecular hydrogen-atom abstraction (k_h) in the radicals (117) and (123) to be $8.3 \times 10^5 sec^{-1}$ and $1.4 \times 10^5 sec^{-1}$ respectively. These are probably the first estimates

of the values of the rate constants of intramolecular hydrogen-atom abstractions (k_h) in ortho-substituted aryl radicals.

Some typical rate constants of radical cyclization reactions (k_c) referred to in the introduction are:-

(a) 5-hexenyl radical[55], $k_c = 1 \times 10^5 sec^{-1}$

(b) 2-(Δ^3-cyclopentenyl)ethyl radical[58], $k_c = 1.9 \times 10^4 sec^{-1}$.

It may be be noted that the estimated rate constants of cyclization that we obtained for aryl radical cyclization reactions are higher than those determined[55,58] for alkyl radicals.

One can discern definite trends in the values of the rate constants of cyclization (k_c) of the aryl radicals which we have examined:-

(a) The o-allyloxyphenyl (108), o-(3-butenyloxy)-phenyl (111), o-(N-allyl-N-methylamino)phenyl (114) and o-[N-(3-butenyl)-N-methylamino]phenyl (117) radicals, in which the sidechains are attached to the aromatic rings by heteroatoms, have higher rate constants of cyclization than the other aryl radicals in which the sidechains are attached to the aromatic rings by carbon atoms.

(b) In the three pairs of homologous aryl radicals (108) and (111), (114) and (117) and finally (120) and

(123), the higher homologue, in which the C=C double bond is in the 6-7 position relative to the radical centre, cyclizes more rapidly than its pair with the double bond in the 5-6 position relative to the radical centre.

(c) It is interesting to note that the radicals (120) and (126), in which the double bonds are in the 5-6 position relative to the radical centre, cyclize more slowly than the radicals (111) and (117) which have the double bonds in the 6-7 position relative to the radical centre.

Conclusions from the results obtained are discussed in the next section.

5.5. CONCLUSIONS

A number of theories have been presented to explain the course of cyclization reactions of alkyl radicals which contain a C=C double bond in the 5-6 position relative to the radical centre. Some of these postulates were put forward before Kochi and Krusic[76] demonstrated that the cyclization of the 5-hexenyl radical can be observed by e.p.r. spectrometry. They showed that the cyclopentylmethyl radical is a discrete intermediate in the cyclization process. This constitutes strong evidence against the theories of Lamb[44] and Walling[56] which invoked the formation of an intramolecular complex between the radical centre and the π-bond followed by direct hydrogen-atom transfer between the radical complex and the hydrogen-atom donor. Moreover we observed the e.p.r. spectra due to the cyclic radical intermediates (85a, b and c) formed by ring closure of ortho-substituted aryl radicals with C=C double bonds in the 5-6 and 6-7 positions relative to the radical centre. On the basis of these e.p.r. observations we can safely exclude the possibility that the stable products of radical cyclization reactions are formed by hydrogen-atom transfer to a complex between the radical centre and the π-bond.

In view of the proposals of Szwarc and Binks[8] concerning the nature of the transition state in the addition of free radicals to double bonds (Chapter 1.2.) it is evident

that for the energetically most favourable process the radical must approach the double bond in a manner that minimizes the diamagnetic repulsion between the two species. If the radical approaches the π -electron cloud of the double bond, as is suggested by the postulates of Lamb[44] and Walling[56], then this diamagnetic repulsion must be at its maximum. It is reasonable then, to assume that the direction of radical attack might be along the C=C axis, or in a direction perpendicular to the nodal plane of the double bond. These processes minimize diamagnetic repulsion[8]. Matsuoka and Szwarc[12] eliminated the possibility of approach along the C=C axis by means of experimental observations which have already been described. Further evidence against radical attack along the C=C axis may be found in the observed[58] cyclization of the 2-(Δ^3-cyclopentenyl)ethyl radical (69) for which attack in that particular direction is sterically not probable. On the other hand approach in a direction perpendicular to the nodal plane of the double bond is possible. Bohm and Abell[13] supported this latter mode of attack, which is consistent with the molecular orbital calculations of Greenwood[14].

In addition to suggesting radical attack in a direction perpendicular to the nodal plane of the C=C double bond and in a line extending almost vertically from the carbon-atom under attack, Struble, Beckwith and Gream[57] advocated initial

interaction between the unpaired electron of the radical centre and the lowest unoccupied π^* orbital of the double bond under attack; these views were also favoured later by Wilt and co-workers[58].

Krusic and Kochi[77] explained the unusually low hyperfine isotropic coupling constants for the β-protons in the e.p.r. spectra of a series of β-heterosubstituted alkyl radicals in terms of incipient 1,3-bonding between the unfilled 3d orbitals of the heteroatom and the p-orbital of the carbon radical centre.

These observations lend support to the proposed[57,58] initial interaction between the carbon radical centre and the unoccupied π^* orbitals in the addition of free radicals to C=C double bonds.

One problem still remains unresolved: the predominant formation of 5-membered ring products on radical cyclization of substrates in which the double bond is in the 5-6 position relative to the radical centre. On the basis that intermolecular radical addition gives the thermodynamically more stable radical intermediate, it has been often suggested that on thermochemical grounds that such a mode of cyclization is anomalous. It has been shown[106] that dicyclohexylformyl peroxide decomposes about 30 times faster than dicyclopentylacetyl peroxide; this large difference in the respective rates of decomposition was attributed[106] to the fact that

the cyclohexyl radical obtained from the former peroxide is more stable than the cyclopentylmethyl radical derived from the latter. Thus it may be said that cyclization to a cyclopentylmethyl radical is an energetically less favourable process than the alternative ring closure to a cyclohexyl radical.

Some light may be shed on the above anomaly by brief consideration of the results and interpretations of a few non-radical cyclization reactions:-

(a) It has been documented[107] that in the ring closure of ω -bromoalkylamines, the irregular trend of rates is due to a combination of more regular trends in activation energy and frequency factor. It was observed that 4-bromobutylamine cyclized 60 times faster than 5-bromopentylamine; a larger frequency factor calculated for the formation of the 5-membered ring was given as the main reason for its more rapid formation. The frequency factor for the formation of a 7-membered ring amine was calculated to be much lower than that for the 6-membered ring amine.

(b) The reaction of glycerol with formaldehyde[108] also brought out some interesting points. Formation of the 5-membered ring acetal was observed to be faster, and this product predominated with short

reaction times; the acetal formation is reversible, and with longer reaction times the 6-membered ring acetal was the major product, since this is the thermodynamically more stable species. Eliel[109] explained these observations in terms of the ease with which the ends of the cyclizing species meet; encounter is more facile for the formation of the 5-membered ring, thus kinetic control over a short period should favour the formation of this compound.

(c) Capon[110] also discussed the factors influencing ring closure. He supported the views of Eliel[109] on the topic, but added that, with increasing length of the chain that is closed, the loss of rotational freedom increases. Thus there is an increasingly unfavourable loss of entropy on ring-closure with increasing ring size.

It may be stated that the arguments of frequency factors, ease with which ends meet and entropy factors as discussed in (a), (b) and (c) actually amount to the same effect. Only the expressions are different.

Julia and Maumy[35] advanced a similar argument to that in (b) to explain their results of the cyclization reactions of alkyl radicals which are stabilized by neighbouring functional groups. They proposed that the cyclization of

radicals containing a C=C double bond in the 5-6 position relative to the radical centre was under kinetic control favouring the formation of 5-membered rings. On the other hand when the conditions were such that the cyclization reaction was reversible, thermodynamic control became predominant leading to the formation of 6-membered rings.

Beckwith[37] suggested that the relative rates of 1,5- and 1,6-cyclization in 5-hexenyl and related radicals depend on thermochemical factors. When both possible processes are highly exothermic and there is a small degree of bond formation in the appropriate transition states, 5-membered ring formation is more rapid, but when the open-chain radical is stabilized by neighbouring substituents and the cyclization processes are less exothermic, 6-membered ring formation becomes more important.

It has been emphasized in the introduction that cyclization reactions of alkyl radicals,which are not stabilized by neighbouring substituents, are irreversible under normal experimental conditions. Some exceptions to this generalization were the observations of Arai[41] and Gordon[42] at high reaction temperatures and the work of Kuivila and his collaborators[60] on the highly strained nortricyclyl radical.

Taking into consideration the foregoing discussion our results may be best interpreted if the following premises are made:

(a) Cyclization reactions of aryl radicals are irreversible under the experimental conditions employed, hence the reactions are governed by kinetic control.

(b) In the initial stages of cyclization there is a loose interaction between the unpaired electron of the radical centre and the lowest unoccupied π^* orbital of the double bond.

(c) The radical centre approaches the double bond in a direction which is perpendicular to the nodal plane of the double bond and in a line extending almost perpendicularly from the carbon atom which is being attacked.

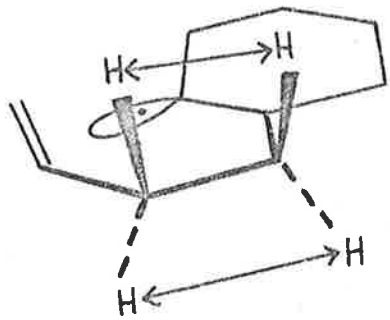
(d) The unpaired electron in each aryl radical resides in an sp^2 hybrid orbital which is in the plane of the benzene ring.

It can be seen by inspection of molecular models representing the radical species that:-

(a) In the 5-membered transition state of the o-allyloxyphenyl radical (108) approach to the more highly substituted carbon-atom is quite facile,

and is free of any steric hindrance.

(b) In the 1,5-ring closure of the o-(3-butenyl)-phenyl radical (126) there is some eclipsing between the hydrogen-atoms of the two methylene groups in the side-chain, resulting in increased 1,2-interactions:-



(c) In the 1,5-ring closure of the o-(N-allyl-N-methylamino)phenyl radical (114) there is again some eclipsing between the N-CH_3 bond and one of the hydrogen-atoms of the neighbouring methylene group, giving rise to a similarly increased 1,2-interaction as in (b).

(d) The approach of the radical centre towards the less highly substituted end of the double bond in the 5-membered transition state of cyclization for the o-vinyloxymethylenephenyl radical (120) is free of the 1,2-interactions mentioned in (b) and (c).

The actual distance from the radical centre of the carbon-atom under attack is, however, somewhat greater than those for the radicals mentioned in (a), (b) and (c).

Thus on the basis of steric interactions it is easy to perceive why the radical (108) cyclizes much more rapidly than the radicals (126) and (114). On the other hand the slower cyclization of the radical (120) than of the three analogous radicals may be attributed to the fact that the radical centre in this transition state is further removed from the carbon-atom which is being approached than in the other three transition states.

The radicals (111), (117) and (123), which contain terminal double bonds in the 6-7 position relative to the respective radical centres, underwent 1,6-ring closure exclusively to give 6-membered ring compounds. Inspection of molecular models of the radical species showed that:-

(a) The 6-membered transition state for the cyclization o-(3-butenyloxy)phenyl radical (111) was free of strain and steric interactions.

(b) The o-[N-(3-butenyl)-N-methylamino]phenyl radical (117) could undergo 1,6-ring closure by means of a transition state which is also free of strain and steric interactions.

(c) Although the o-allyloxymethylenephenyl radical (123)

was free of steric interactions in the 6-membered transition state for ring closure, the distance between the radical centre and the carbon atom under attack was somewhat larger than for the radicals (111) and (117).

On the basis of the distances of the respective radical centres from the carbon-atoms under attack it is clear why the radical (123) cyclizes at the slowest rate amongst these three radicals. It is also clear why intramolecular hydrogen-atom abstraction can be a competing reaction with the cyclization step. It is not clear, however, why (111) cyclizes more slowly than (117) and yet undergoes no intramolecular hydrogen-atom abstraction.

A molecular model of the o-vinyloxyphenyl radical (129) indicates that in the 5-membered transition state required for ring closure the distance between the radical centre and the terminal carbon atom of the sidechain is much larger than in any of the previous cases. It is not surprising, therefore, that cyclization did not take place in this system.

Two factors seem to emerge from correlation of the relative rate constants of cyclization and the favourability of the corresponding transition states for the cyclizations. The rate constant is sensitive to steric interactions and also

to variations in the distance between the radical centre and the carbon atom under attack. Heusler and Kalvoda[111] have demonstrated the extreme importance of a favourable geometry in the transition state for intramolecular transfer of hydrogen from carbon to oxygen.

It is possible to explain why the rate constants of cyclization of the aryl radicals, which we have examined, are higher than those reported for alkyl radicals, especially for those aryl radicals which contain the terminal double bond in the 6-7 position relative to the radical centre. For the first part of this explanation it is useful to reiterate the proposal of Capon[110] which states that, with increased loss of rotational freedom of a molecule, there will be an increasingly unfavourable loss of entropy on ring closure. Even in the o-(3-butenyl)phenyl radical (126) there may be a smaller loss of rotational freedom than in the analogous 5-hexenyl radical, since in the former there is no rotation about the C_1-C_2 bond relative to the radical centre. When the ortho-substituents are attached to the benzene ring by means of an oxygen-atom as in radicals (108) and (111) or a nitrogen-atom as in radicals (114) and (117) there may be an even smaller loss of rotational freedom in the transition state, since the conjugation of the lone pairs of electrons of the heteroatoms with the benzene ring restricts

rotation about these bonds.

An additional line of argument involves the application of Hammond's postulate[112], which states that for highly exothermic reactions the transition state resembles the starting materials, and for endothermic reactions the transition state resembles the products. For example Matsuoka and Szwarc[12] showed experimentally that in the transition state of the addition of methyl radicals to the double bond in styrene, a highly exothermic reaction, the incipient C-CH_3 bond is comparatively long; in other words the transition state resembles starting materials.

The stabilities of cycloalkylmethyl radicals, formed either by alkyl radical or by aryl radical cyclization reactions, should be about the same. Thus the relative exothermicities of the respective reactions will depend on the relative strengths of the new C-C bonds which are formed during the cyclization process. Benson[113] quotes the dissociation energies of the benzene-isopropyl and n-propyl-isopropyl bonds as being 87.5 and 80 kcal/mole respectively; the strengths of these bonds would be expected to approximate to the strengths of the bonds formed by radical attack at the more highly substituted end of the terminal double bonds in the cyclization reactions of aryl and alkyl radicals respectively. Thus to a first degree of approximation it can be assumed that the 7.5 kcal/mole difference between the

bond dissociation energies quoted above represents the amount by which aryl radical cyclization reactions are more exothermic than the ring closure of the alkyl analogues. In terms of Hammond's postulate this means that, in the transition states of the intramolecular cyclization reactions, the incipient C-C bonds will be longer than those of the analogous alkyl radical reactions. In other words this implies that the faster rate of these reactions is due to lower losses of entropy in the transition states.

We have demonstrated that intramolecular cyclization reactions of aryl radicals, with ortho substituents containing C=C double bonds in the 5-6 or 6-7 position relative to the radical centre, occur with great ease. We have also been able to confirm that the reduction of aryl iodides with tri-n-butylstannane proceeds by a radical mechanism. From accurate product studies we were able to estimate the rate constants of these aryl radical cyclization reactions, and to establish, in agreement with the results of other workers for the analogous alkyl radical cyclization reactions, that such intramolecular aryl radical ring closure reactions occur by radical attack at that end of the terminal C=C bond which is nearer to the benzene ring. We were able to estimate the rate constants of two intramolecular hydrogen-atom abstraction reactions of aryl

radicals; these probably constitute the only quantitative data available for such reactions. Furthermore by e.p.r. investigations we have observed the spectra due to the cyclic radical intermediates of intramolecular aryl radical cyclization reactions.

Further work that could be done in order to complete these investigations should include determination of the absolute rates of reduction of ortho-substituted aryl iodides and measurements of the rate constants of hydrogen-atom abstraction from tri-n-butylstannane by the aryl radicals formed in these reductions. Such determinations could be carried out by means of calorimetric methods in conjunction with the rotating sector technique[55]. The knowledge of these rate constants should enable more accurate estimations of the rate constants of cyclization in the reactions discussed above.

PART III

CHAPTER 6

EXPERIMENTAL

6.1. PREAMBLE

General

Melting points were determined using a Kofler hot stage and are uncorrected.

Microanalyses were carried out by the Australian Micro-Analytical Service, Melbourne.

Purification by column chromatography was achieved using 1 part of product to 50 parts of support.

Spectroscopic

Infrared spectra were determined on liquid films, unless otherwise stated, using a Perkin-Elmer 237 Grating Spectrophotometer.

Nuclear magnetic resonance spectra were recorded with Varian DP60 or T60 spectrometers at 60 MHz. The spectra were determined in carbon tetrachloride solution and chemical shifts were measured relative to tetramethyl silane as internal standard. The range of chemical shifts of multiplets (m), in parts per million, are given to the first decimal place. The chemical shifts of singlets (s), doublets (d), triplets (t) and doublets of doublets (dd) are given, in parts per million, to the second decimal

place. Coupling constants (J) are given to the nearest 0.5 Hz.

Electron paramagnetic resonance spectra were recorded on a Varian E9 spectrometer (for details see later).

Mass spectra were determined on a Hitachi-Perkin-Elmer RMU-6D double focusing spectrometer.

Gas liquid chromatography

Routine purity checks were carried out using Perkin-Elmer 801 and 881 instruments; the latter was equipped with a Perkin-Elmer 194B printing integrator. Both employed flame ionization detectors, and nitrogen was used as the carrier gas at a flowrate of 30ml/min in all instances. Preparative separations were achieved by the use of a Varian-Aerograph A705 instrument fitted with a flame ionization detector using nitrogen as the carrier gas.

Quantitative analyses were carried out with the aid of calibration graphs obtained by analysing, under indentical conditions, accurately made mixtures of an internal standard and independently synthesised products (for details see later).

Routine purity checks are indicated in the text as, for example, G.C.$_{120^{o}}^{A}$; this means column A was used at a temperature of 120°.

The list of columns used:-

A Carbowax 20M (10% on Aeropak 30 solid support of mesh size 100-120) in 20ft x $\frac{1}{8}$in. stainless steel tubing.

B P.D.E.A.S. (3% on Aeropak 30 solid support of mesh size 100-120) in 14ft x $\frac{1}{8}$in. glass tubing.

C S.E.52 (10% on Aeropak 30 solid support of mesh size 100-120) in 6ft x $\frac{1}{8}$in. stainless steel tubing.

D Nitril gum (3% on Aeropak 30 solid support of mesh size (100-120) in 20ft x $\frac{1}{8}$in. stainless steel tubing.

Solvents

Diethyl ether was distilled from phosphorous pentoxide, and stored over sodium wire. It was redistilled from lithium aluminium hydride immediately before use.

Tetrahydrofuran was fractionated and stored on 4 Angstrom molecular sieves. It was redistilled from lithium aluminium hydride prior to use.

Diethyleneglycol dimethyl ether was stored over calcium hydride. It was redistilled under reduced pressure from lithium aluminium hydride before use.

Dimethyl formamide was fractionated and stored over 4 Angstrom molecular sieves.

Acetone was purified by distillation.

Chloroform, methylene chloride, light petrol (b.p. 50-60^{o}), hexane and pentane were all dried over calcium chloride

and distilled.

Carbon tetrachloride (reagent grade) was distilled.

Cyclohexane (reagent grade) was distilled from calcium hydride.

Benzene (reagent grade) was distilled from calcium hydride.

Starting materials

All alkyl halides used were stored over 4 Angstrom molecular sieves and distilled before use.

Commercially available starting materials were either of reagent grade or were purified in the appropriate manner until they contained less than 1% impurity.

6.2. PREPARATION OF ARYL IODIDES AND THEIR EXPECTED PRODUCTS FROM THE TRI-n-BUTYLSTANNANE REDUCTIONS

Allyloxybenzene (92a)

Allyl bromide (33.0g, 0.25mole) was added dropwise to a stirred mixture of phenol (23.5g, 0.25mole) and anhydrous potassium carbonate (38.5g, 0.25mole) in acetone (200ml) at a rate that maintained the reaction mixture at gentle reflux. The reaction mixture was heated under reflux for 8 hr., then cooled, diluted with water (500ml) and extracted with ether (3 x 100ml). The combined ether layers were washed with 10% aqueous sodium hydroxide solution (6 x 100ml), water and saturated brine, dried ($MgSO_4$) and concentrated to give a liquid which was chromatographed on basic alumina with petrol and ether mixtures as the eluants. On removal of the solvent the residue was distilled under reduced pressure to give allyloxybenzene as a colourless liquid (13.0g, 40%), b.p. 79°/12mm (lit.[114] b.p. 73°/11mm), ν_{max} 3070 and 3030 ($CH=CH_2$), 1640 (olefinic C=C), 1230 (C-O), 980 and 915 ($CH=CH_2$), 750 and 690cm^{-1} (aromatic monosubstitution), δ 7.4 - 6.6 (m, 5H, aromatic H), 6.3 - 5.6 (m, 1H, $C\underline{H}=CH_2$), 5.5 - 5.0 (m, 2H, $CH=C\underline{H}_2$) and 4.5 - 4.3 (m, 2H, $O-C\underline{H}_2$), G.C.$^{A}_{130°}$ one peak.

o-Alloxyiodobenzene (88a)

When o-iodophenol was treated with allyl bromide, using

the same procedure as described above for the preparation of (92a), o-allyloxyiodobenzene was obtained as a colourless liquid (48%), b.p. 141-144°/18mm. (Found: C, 41.5; H, 3.4; I, 48.5. C_9H_9IO requires C, 41.6; H, 3.5; I, 48.8%), ν_{max} 3070 and 3020 ($CH=CH_2$), 1645 (olefinic C=C), 1245 (C-O), 990 and 925 ($CH=CH_2$) and 745cm^{-1} (aromatic 1,2 disubstitution), δ 7.9 - 6.2 (m, 4H, aromatic H), 6.2 - 5.5 (m, 1H, $CH=CH_2$), 5.5 - 5.0 (m, 2H, $CH=CH_2$) and 4.7 - 4.3 (m, 2H, $O-CH_2$), m/e 260, G.C.$^{A}_{135°}$ one peak.

3-Methylbenzofuran

The sequence described in Organic Syntheses[115] was used without modification.

(a) Ethyl α-chloroacetoacetate was obtained as a slightly yellowish liquid (93%) b.p. 85-89°/17mm (lit.[115] b.p. 85-89°/17mm).

(b) Ethyl α-phenoxyacetoacetate was prepared from ethyl α-chloroacetoacetate and sodium phenoxide and used in the next step without purification.

(c) Ethyl 3-methylcoumarilate was obtained, from cyclization of ethyl α-phenoxyacetoacetate, as a colourless liquid (53%), b.p. 128°/1.8mm (lit.[115] b.p. 162-167°/16mm).

(d) 3-Methylcoumarilic acid, obtained by hydrolysis of the above ester, was a colourless crystalline solid (74%), m.p. 192-193° (lit.[115] m.p. 192-193°).

Decarboxylation of 3-methylcoumarilic acid at 280° gave

liquid which was fractionated to give 3-methylbenzofuran as a colourless liquid (86%), b.p. 195-197° (lit.[115] b.p. 195 - 197°), ν_{max} 1450 (CH_3), 1280 (C-O) and 740cm^{-1} (aromatic 1,2 disubstitution), δ 7.5 - 6.9 (m, 5H, aromatic H) and 2.10 (d, 3H, J=1.5 Hz, CH_3), G.C.$^{A}_{135}$° one peak.

3-Methyl-2,3-dihydrobenzofuran (93a)

The method described by Alexander[83] for the reduction of benzofuran was modified in the following manner:- The reaction vessel consisted of two 100ml round bottom flasks, connected at the 50ml mark by means of a short glass tube, with their respective ground joints parallel. Bulb A was fitted with a reflux condenser carrying a drying tube, whilst bulb B was fitted with a ground glass stopper. Sodium (2.0g) was introduced into bulb B, and 3-methylbenzofuran (1.0g) in absolute ethanol (5ml) was placed into bulb A. The reaction vessel was placed into a boiling water bath with both necks vertical. When the sodium was molten, the boiling solution in bulb A was tipped into bulb B, and the resulting mixture was heated under reflux in the water bath until the mixture became viscous. The apparatus was then brought back to its original position and ethanol (5ml) was introduced through the condenser into bulb A, brought to the boil and tipped into bulb B. The reaction mixture was again heated under reflux until it became viscous. This last procedure was repeated several times until all the sodium had

reacted. The reaction mixture was then poured into water (150ml) and extracted with ether (3 x 50ml). The combined ether layers were washed with saturated brine, dried ($MgSO_4$), concentrated, and distilled to give 3-methyl-2,3-dihydrobenzofuran as colourless liquid (0.88g, 88%), b.p. 78°/12mm (lit.[116] b.p. 86-87°/16mm), ν_{max} 1460 (CH_3), 1225 (C-O) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.3 - 6.6 (m, 4H, aromatic H), [4.60 (m, 1H), 4.00 (m, 1H), 3.45 (m, 1H) and 1.30 (d, 3H), O-CH_2-CH-CH_3, $ABXY_3$, J_{AB}= 8.5, J_{AX}=9.0, J_{BX}=7.0 and J_{XY_3}=7.0 Hz], G.C.$^{A}_{130^o}$ one major peak (>99%) and one small peak (<1%) (3-methylbenzofuran).

Chroman (94a)

The reaction sequence of Deady et.al.[117] was used:-

1,3-Diphenoxypropane was obtained as a colourless crystalline solid (84%), m.p. 60° (lit.[117] m.p. 60°). Cyclization of 1,3-diphenoxypropane with anhydrous aluminium chloride gave, after distillation, chroman as a colourless liquid (84%), b.p. 94-95°/12mm (lit.[117] b.p. 96-100°/16mm), ν_{max} 1225 (C-O) and 750cm^{-1} (aromatic 1,2-disubstitution), δ 7.0 - 6.4 (m, 4H, aromatic H), 4.02 (t, 2H, J=5 Hz, O-CH_2), 2.67 (t, 2H, J=6 Hz, benzylic CH_2) and 2.1 - 1.6 (m, 2H, CH_2), G.C.$^{A}_{130^o}$ one peak.

(3-Butenyloxy)benzene (92b)

A mixture of 4-bromo-1-butene (7.42g) and sodium phenoxide (5.80g) in water (60ml) were boiled under reflux for 3.5hr.

The reaction mixture was cooled, diluted with water and extracted with ether several times. The combined ether layers were washed with 10% aqueous sodium hydroxide solution, water and saturated brine, dried ($MgSO_4$), and concentrated to yield a liquid (5.74g). This crude product was purified by chromatography on basic alumina with light petrol as the eluant. The eluate was concentrated and distilled under reduced pressure to give (3-butenyloxy)benzene as a colourless liquid (3.07g, 42%), b.p. 130 - 131°/72mm (lit.[118] b.p. 209°/760mm), ν_{max} 3070 and 3040 ($CH=CH_2$), 1640 (olefinic C=C), 1235 (C-O), 985 and 910 ($CH=CH_2$), 750 and 685cm^{-1} (aromatic monosubstitution), δ 7.4 - 6.6 (m, 5H, aromatic H), 6.3 - 5.5 (m, 1H, $C\underline{H}=CH_2$), 5.3 - 4.8 (m, 2H, $CH=C\underline{H}_2$), 3.87 (t, 2H, J=6.5 Hz, $O-CH_2$) and 2.7 - 2.2 (m, 2H, allylic CH_2), G.C.$^{A}_{130^o}$ one peak.

o-(3-Butenyloxy)iodobenzene (89a)

A mixture of o-iodophenol (4.36g), sodium hydroxide (0.80g) and 4-bromo-1-butene (2.80g) in water (20ml) was heated under reflux for 5 hr. The cold reaction mixture was diluted with water, and extracted with ether several times. The combined ether layers were washed with 10% aqueous sodium hydroxide solution, water and saturated brine, dried ($MgSO_4$) and concentrated to give a liquid. This crude product was chromatographed on basic alumina with light petrol and ether mixtures as the eluants. The eluate

was concentrated and distilled under reduced pressure to give o-(3-butenyloxy)iodobenzene as a colourless liquid (3.11g, 57%), b.p. 146-148°/13mm, (Found: C, 43.9; H, 4.0; I, 46.4. $C_{10}H_{11}IO$ requires C, 43.8; H, 4.0; I, 46.3%), ν_{max} 3060 and 3020 ($CH=CH_2$), 1645 (olefinic C=C), 1245 (C-O), 980 and 915 ($CH=CH_2$) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.8 - 6.4 (m, 4H, aromatic H), 6.4 - 5.6 (m, 1H, $C\underline{H}=CH_2$), 5.4 - 4.9 (m, 2H, $CH=C\underline{H}_2$), 3.97 (t, 2H, J=7 Hz, $O-C\underline{H}_2$) and 2.8 - 2.4 (m, 2H, allylic $C\underline{H}_2$), m/e 274, G.C.$^{B}_{130}$o one peak.

3-Phenoxypropionic acid

The method described by Powell[119] was used to prepare 3-phenoxypropionic acid as a colourless crystalline solid (10%), m.p. 98° (lit.[119] m.p. 98°).

4-Chromanone

3-Phenoxypropionic acid was cyclized in polyphosphoric acid using the procedure described by Parham and Huestis[120] to give, after distillation under reduced pressure, 4-chromanone as a colourless liquid (51%), b.p. 77-79°/0.25mm (lit.[120] b.p. 78-80°/0.30mm).

4-Methylchroman (93b)

(a) 4-Methyl-4-chromanol

Methyl iodide (3.0g) in dry ether (10ml) was added dropwise to a stirred suspension of magnesium turnings (0.48g) in dry ether (10ml) at a rate that maintained the reaction

mixture at gentle reflux. The reaction mixture was then stirred at room temperature for 2 hr. A solution of 4-chromanone (1.98g) in dry ether (20ml) was added dropwise, with stirring, to the reaction mixture so that it was maintained at gentle reflux. The reaction mixture was stirred at room temperature for 2 hr., then an excess of a saturated aqueous solution of ammonium chloride was added, and the resulting mixture stirred at room temperature for 1 hr. After filtration the ethereal layer was separated and the aqueous layer was extracted with ether (3 x 20ml). The combined ether layers were washed with saturated brine, dried (Na_2SO_4) and concentrated to give the required alcohol (1.42g) which was used in the next step without purification.

(b) 4-Methyl-4-chromanol (1.42g) from the previous preparation was dissolved in ethanol (50ml) and platinum oxide (0.05g) was added. This mixture was shaken under an atmosphere of hydrogen until no more hydrogen was absorbed, then filtered through a pad of Celite, concentrated and distilled under reduced pressure to give 4-methylchroman as a colourless liquid (1.40g, 70% overall yield), b.p. 102-104°/13mm (lit.[121] b.p. 80-90°/5mm), ν_{max} 1460 (CH_3), 1230 (C-O) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.1 - 6.5 (m, 4H, aromatic H), 4.05 (t, 2H, J=5 Hz, O-CH_2), 3.1 - 2.5 (m, 1H, CH), 2.3 - 1.4 (m, 2H, CH_2) and 1.25 (d, 3H, J= 7 Hz, CH_3), G.C.$^{D}_{120}$° one peak.

2,3,4,5-Tetrahydro-1-benzoxepin (94b)

The procedure described by Baddeley et.al.[122] was used to prepare 2,3,4,5-tetrahydro-1-benzoxepin as a colourless liquid, which solidified on standing, b.p. 90-92°/9mm (lit.[122] b.p. 86-88°/7mm), ν_{max} (CCl_4), 1230 (C-O) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.2 - 6.5 (m, 4H, aromatic H), 4.2 - 3.8 (m, 2H, O-CH_2), 3.0 - 2.6 (m, 2H, benzylic CH_2) and 2.2 - 1.6 (m, 4H, CH_2-CH_2), G.C. $^{D}_{120°}$ one peak.

N-Allyl-N-methylaminobenzene (92c)

This reaction represents the standard alkylation procedure used for the preparation of all of the tertiary amines from secondary amines.

A stirred mixture of N-methylaminobenzene (16.05g, 0.15 mole), allyl bromide (27.23g, 0.225mole) and anhydrous sodium carbonate (9.54g, 0.09mole) in a 4:1 ethanol-water mixture (75ml) was boiled under reflux overnight. Most of the ethanol and excess allyl bromide was then removed on a rotary film evaporator under reduced pressure. The residue was diluted with water (100ml) and extracted with ether (3 x 50ml). The combined ether layers were washed with water and saturated brine, dried ($NaSO_4$) and concentrated to give a liquid. This crude product was chromatographed on silica gel with light petrol and ether mixtures as the eluants. The eluate was concentrated and distilled under reduced pressure to give N-allyl-N-methylaminobenzene as a

colourless liquid (11.84g, 54%), b.p. 118-120°/25mm (lit.[123] b.p. 216-217°/760mm), ν_{max} 3070 and 3030 ($CH=CH_2$), 2810 ($N-C\underline{H}_3$), 1645 (olefinic C=C), 1350 (C-N), 985 and 910 ($CH=CH_2$), 740 and 685cm^{-1} (aromatic monosubstitution), δ 7.3 - 6.5 (m, 5H, aromatic H), 6.2 - 5.5 (m, 1H, $C\underline{H}=CH_2$), 5.3 - 4.8 (m, 2H, $CH=C\underline{H}_2$), 3.9 - 3.7 (m, 2H, $N-CH_2$) and 2.83 (s, 3H, $N-CH_3$), G.C.$^{B}_{100}$° one peak.

1,3-Dimethylindole

The method described by Rees and Smithen[124] was used to prepare 1,3-dimethylindole as a slightly yellowish liquid b.p. 66-67°/0.35mm (lit.[124] b.p. 72-73°/0.4mm), δ 7.5 - 6.7 (m, 4H, aromatic H), 6.50 (s, 1H, pyrrole ring H), 3.45 (s, 3H, $N-CH_3$) and 2.25 (s, 3H, $C-CH_3$), G.C.$^{B}_{100}$° one peak.

1,3-Dimethylindoline (93c)

The procedure described by Smith and Utley[89] for the catalytic reduction of 3-methylindole to 3-methylindoline was used for the reduction of 1,3-dimethylindole to give 1,3-dimethylindoline as a colourless liquid (97%) b.p. 110°/21mm, ν_{max} 2960 and 2860 ($C-C\underline{H}_3$), 2800 ($N-C\underline{H}_3$), 1460 and 1365 ($C-C\underline{H}_3$), 1320 (C-N) and 735cm^{-1} (aromatic 1,2-disubstitution), δ 7.1 - 6.0 (m, 4H, aromatic H), 3.6 - 2.8 (m, 3H, $N-C\underline{H}_2-C\underline{H}$), 2.65 (s, 3H, $N-CH_3$) and 1.25 (d, 3H, J=6 Hz, $C-CH_3$), G.C.$^{B}_{100}$° one major peak (>99%) and one small peak (<1%), picrate m.p. 110-111° (lit.[125] m.p. 111-112°).

N-methyl-1,2,3,4-tetrahydroquinoline (94c)

A stirred mixture of 1,2,3,4-tetrahydroquinoline (19.95g), methyl iodide (31.95g) and sodium carbonate (9.54g) in 4:1 ethanol-water mixture (75ml) was boiled under reflux overnight, then worked-up by the standard procedure to give N-methyl-1,2,3,4-tetrahydroquinoline as a colourless liquid, b.p. 127-129°/22mm (lit.[126] b.p. 112°/3.5mm), ν_{max} 2810 (N-CH_3), 1310 (C-N) and 740cm^{-1} (aromatic 1,2-disubstitution), δ 7.0 - 6.1 (m, 4H, aromatic H), 3.3 - 3.0 (m, 2H, N-CH_2), 2.80 (s, 3H, N-CH_3), 2.70 (t, 2H, J=7 Hz, benzylic CH_2) and 2.1 - 1.6 (m, 2H, CH_2), G.C.$^{B}_{100°}$ one major peak (> 99%) and one small peak (< 1%).

o-(N-Formylamino)iodobenzene

The method described[127] for the formylation of o-aminoethylbenzene was modified in the following way:-

A mixture of o-aminoiodobenzene (43.80, 0.20mole) and 99% formic acid (25g) in dry benzene (200ml) was boiled under reflux with a Dean-Stark water separator attached. When no more water was being collected the separator was emptied and a further portion of 99% formic acid (25g) was added to the reaction mixture, which was again boiled under reflux until no more water was being collected in the separator. The benzene and the residual formic acid were then removed under pressure on a rotary film evaporator and the solid residue was recrystallised from a mixture of hexane and methylene

chloride to give yellowish crystals of o-(N-formylamino)-iodobenzene (33.6g, 67%) m.p. 110-111.5°. A small sample was recrystallised to constant melting point, m.p. 113-113.5° (lit.[128] m.p. 113-113.5°).

o-(N-Methylamino)iodobenzene

The general procedure described by Brown and Heim[87] for the reduction of carboxamides to amines with diborane was modified in the following manner:-

Diborane was generated, under an atmosphere of high purity nitrogen, by the slow addition, during 4 hr., of a saturated solution of iodine (63.5g) in dry diethyleneglycol dimethyl ether to a stirred suspension of sodium borohydride (19g) in dry diethyleneglycol dimethyl ether (500ml). The nascent diborane was bubbled into a stirred solution of o-(N-formylamino)iodobenzene (30.9g) in dry tetrahydrofuran (250ml) which was kept at 0° under an atmosphere of high purity nitrogen. When the addition of the iodine solution was complete, the contents of the diborane generator were heated to and then kept at 70-80° for 1.5 hr. in order to drive over the last traces of diborane into the reaction mixture. A ground glass stopper was then substituted for the diborane inlet tube in the reaction vessel and the ice bath was removed. The reaction mixture, still under an atmosphere of nitrogen, was then boiled under reflux for 2 hr., then cooled to room temperature and

allowed to stand overnight. The reaction mixture was then cooled to 0° and aqueous hydrochloric acid solution (40ml, 6N) was added dropwise with stirring. When the addition was complete, the reaction mixture was allowed to warm up to room temperature, and was then heated slowly to 60°. When no more hydrogen was being evolved, the reaction mixture was allowed to cool to room temperature, and the solvent was removed under vacuum (30mm) with the aid of gentle heating. The residue was then made alkaline by the dropwise addition of 10% aqueous sodium hydroxide solution and extracted with methylene chloride (3 x 200ml). The combined methylene chloride layers were washed with water, dried (Na_2SO_4) and concentrated under reduced pressure to give a dark red oil (29.62g). The crude product was immediately chromatographed on silica gel (1500g) using hexane and ether mixtures as the eluants. The progress of the elution was followed by gas chromatography. On concentration of the eluate o-(N-methylamino)iodobenzene was obtained as a slightly yellowish liquid (25.49g, 88%). A small sample was distilled under reduced pressure giving o-(N-methylamino)iodobenzene as a colourless liquid b.p. 108-110°/4.5mm, (Found: C, 36.4; H, 3.4; N, 6.1. C_7H_8NI requires C, 36.1; H, 3.5; N, 6.0%), ν_{max} 3420 (N-H), 2815 (N-CH_3), 1310 (C-N) and 735cm^{-1} (aromatic 1,2-disubstitution), δ 7.7 - 6.2 (m, 4H, aromatic H), 4.4 - 3.7 (m, 1H, NH) and 2.85 (s, 3H, N-CH_3), m/e 233, G.C.$^{B}_{130°}$ one peak.

o-(N-allyl-N-methylamino)iodobenzene (88b)

A mixture of o-(N-methylamino)iodobenzene (2.33g), allyl bromide (1.34g) and sodium carbonate (0.64g) in 4:1 ethanol-water mixture (5ml) was boiled under reflux with stirring for 24 hr. A small sample was then withdrawn and worked-up in the standard manner. Analysis by gas chromatography indicated the presence of a small amount of the starting amine. Allyl bromide (0.45g) and sodium carbonate (0.23g) were added to the reaction mixture and boiling under reflux was continued for a further 24 hr. The reaction mixture was then worked-up in the standard manner giving, after distillation under reduced pressure, o-(N-allyl-N-methyl-amino)iodobenzene as a colourless liquid (1.75g, 64%), b.p. 83°/2mm, (Found: C, 44.2; H, 4.4. $C_{10}H_{12}IN$ requires C, 44.0; H, 4.4%), ν_{max} 3090 and 3020 (CH_2=CH), 2800 (N-CH_3), 1645 (olefinic C=C), 1350 (C-N), 995 and 910 (CH_2=CH) and 755cm^{-1} (aromatic 1,2-disubstitution), δ 7.9 - 6.2 (m, 4H, aromatic H), 6.2 - 5.6 (m, 1H, C<u>H</u>=CH_2), 5.4 - 4.9 (m, 2H, CH=C<u>H</u>$_2$), 3.7 - 3.3 (m, 2H, N-CH_2) and 2.65 (s, 3H, N-CH_3), m/e 273, G.C.$^{B}_{130°}$ one peak.

N-(3-butenyl)-N-methylaminobenzene (92d)

A stirred mixture of N-methylaminobenzene (8.025g), 4-bromo-1-butene (13.5g) and sodium carbonate (4.77g) in 4:1 ethanol-water mixture (40ml) was boiled under reflux over-night. The reaction mixture was worked-up by the standard

procedure, and gave, after distillation under reduced pressure, N-(3-butenyl)-N-methylaminobenzene as a colourless liquid (9.45g, 59%), b.p. 114°/12mm, (Found: C, 81.7; H, 9.4. $C_{11}H_{15}N$ requires C, 81.9; H, 9.4%), ν_{max} 3070 and 3030 (CH_2=CH), 2810 (N-CH_3), 1635 (olefinic C=C), 1340 (C-N), 980 and 905 (CH_2=CH), 740 and 690cm^{-1} (aromatic mono-substitution), δ 7.3 - 6.4 (m, 5H, aromatic H), 6.1 - 5.4 (m, 1H, C$\underline{H}$=CH_2), 5.3 - 4.8 (m, 2H, CH=C$\underline{H}_2$), 3.5 - 3.2 (m, 2H, N-CH_2), 2.90 (s, 3H, N-CH_3) and 2.5 - 2.0 (m, 2H, allylic CH_2), m/e 161, G.C.$^{B}_{100}$° one peak.

o-[N-(3-butenyl)-N-methylamino]iodobenzene (89b)

A mixture of o-(N-methylamino)iodobenzene (4.61g), 4-bromo-1-butene (3.60g) and sodium carbonate (1.28g) in 4:1 ethanol-water mixture (10ml) was boiled under reflux overnight. A small sample was then withdrawn and worked-up in the usual manner. Analysis by gas chromatography indicated the presence of starting amine. Sodium carbonate (1.28g) and 4-bromo-1-butene (3.60g) were then added to the reaction mixture and boiling under reflux was continued for 14 days. From time to time samples were withdrawn and analysed by gas chromatography. At the end of 14 days some starting amine was found to by present. Further portions of 4-bromo-1-butene (2.40g), sodium carbonate (0.85g) and 4:1 ethanol-water mixture (5ml) were then added to the reaction mixture and boiling under reflux was continued for another 7 days.

At the end of this period, analysis by gas chromatography indicated the absence of the starting amine. The reaction mixture was worked-up in the standard manner and after distillation gave o-[N-(3-butenyl)-N-methylamino]iodobenzene as a colourless liquid (4.05g, 72%), b.p. 113°/2.5mm, (Found: C, 45.7; H, 5.0. $C_{11}H_{14}IN$ requires C, 46.0; H, 4.9%), ν_{max} 3080 and 3010 (CH_2=CH), 2800 (N-CH_3), 1645 (olefinic C=C), 1370 (C-N), 980 and 910 (CH_2=CH) and 755cm^{-1} (aromatic 1,2-disubstitution), δ 7.9 - 6.6 (m, 4H, aromatic H), 6.2 - 5.5 (m, 1H, C<u>H</u>=CH_2), 5.2 - 4.8 (m, 2H, CH=C<u>H</u>$_2$), 3.2 - 2.8 (m, 2H, N-CH_2), 2.70 (s, 3H, N-CH_3) and 2.5 - 2.0 (m, 2H, allylic CH_2), m/e 287, G.C.$^{B}_{130}$° one peak.

1-Formyl-4-methyl-1,2,3,4-tetrahydroquinoline

The method described by Yudin et.al.[88] for the conversion of 2-methylquinoline to 1-formyl-2-methyl-1,2,3,4-tetrahydroquinoline, was used unmodified to prepare from 4-methylquinoline the required 1-formyl-4-methyl-1,2,3,4-tetrahydroquinoline as a colourless liquid (70%), b.p. 168°/12mm, (Found: C, 75.2; H, 7.5; N, 7.9. $C_{11}H_{13}NO$ requires C, 75.4; H, 7.5; N, 8.0%), ν_{max} 1665 (C=O) and 750cm^{-1} (aromatic 1,2-disubstitution), δ 8.55 (s, 1H, O=C-H), 7.5 - 6.8 (m, 4H, aromatic H), 4.0 - 3.4 (m, 2H, N-CH_2), 3.2 - 2.5 (m, 1H, benzylic CH), 2.4 - 1.4 (m, 2H, CH_2) and 1.30 (d, 2H, J=6 Hz, CH_3), m/e 175.

1,4-Dimethyl-1,2,3,4-tetrahydroquinoline (93d)

A solution of 1-formyl-4-methyl-1,2,3,4-tetrahydroquinoline (10.30g, 0.061mole) in dry ether (180ml) was added dropwise to a stirred suspension of lithium aluminium hydride (3.80g) in dry ether (360ml) under an atmosphere of pure nitrogen. When the addition was complete, the stirred reaction mixture was boiled under reflux for 15 hr. The reaction mixture was then cooled to 0° and, with stirring, water (4ml) was added dropwise followed by 15% aqueous sodium hydroxide (4ml) then water (12ml). The resulting mixture was stirred at 0° for 30 min., then filtered. The filtrate was dried (Na_2SO_4), concentrated and the crude product chromatographed on silica gel with light petrol-ether mixtures as the eluants. The eluate was concentrated and distilled under reduced pressure to give 1,4-dimethyl-1,2,3,4-tetrahydroquinoline (8.35g, 88%), b.p. 122°/12mm (lit.[129] b.p. 145°/25mm), ν_{max} 2810 (N-CH_3), 1325 (C-N) and 740cm^{-1} (aromatic 1,2-disubstitution), δ 7.1 - 6.3 (m, 4H, aromatic H), 3.3 - 2.9 (m, 2H, N-CH_2), 2.80 (s, 3H, N-CH_3), 2.7 - 1.4 (m, 3H, CH-CH_2) and 1.25 (d, 3H, J= 7 Hz, C-CH_3), G.C.$^{B}_{120}$° one peak.

Homodihydrocarbostyril

The method described by Conley[130] for the Beckmann rearrangement of 1-tetralone with sodium azide in polyphosphoric acid was used to prepare homodihydrocarbostyril

as a colourless crystalline solid, m.p. 141-142° (lit.[130] m.p. 141-142°).

2,3,4,5-Tetrahydro-1-benzazepine

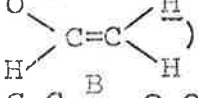
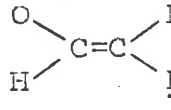
The method for the reduction of a solid secondary amide described by Wilson and Steinberg[131] was adapted:-

Homodihydrocarbostyril (20.12g, 0.125mole) was placed in a "Soxhlet" extractor fitted with an ether condenser carrying a drying tube. Lithium aluminium hydride (8.00g, 0.173mole) in dry ether (800ml) was stirred in a 2 litre round bottom flask which was attached to the extractor by means of a ground glass joint. The contents of the flask were heated under reflux with stirring for 5 hr., then the resulting reaction mixture left at room temperature overnight. The residual starting amide (2.00g) was removed from the extractor, and the stirred reaction mixture was treated dropwise at 0° consecutively with water (8ml), 15% aqueous sodium hydroxide (8ml) and water (24ml). After stirring at 0° for a further 30 min., the reaction mixture was filtered. The ethereal solution dried (Na_2SO_4), concentrated, and the crude product was chromatographed on silica gel using light petrol-ether mixtures as the eluants. The eluate was concentrated to give 2,3,4,5-tetrahydro-1-benzazepine as a yellowish liquid (16.56g, quant.) which solidified on standing, m.p. 32° (lit.[132] m.p. 32°), G.C.$^{B}_{120°}$ one peak.

1-Methyl-2,3,4,5-tetrahydro-1-benzazepine (94d)

A stirred mixture of 2,3,4,5-tetrahydro-1-benzazepine (7.3g) and methyl iodide (9.5g) and sodium carbonate (3.18g) in 4:1 ethanol-water mixture (40ml) was boiled under reflux overnight. The reaction mixture was worked-up in the standard manner and distilled under reduced pressure to give 1-methyl-2,3,4,5-tetrahydro-1-benzazepine as a colourless liquid (5.60g, 75%), b.p. 114°/12mm (lit.[133] b.p. 116-117°/15mm), ν_{max} 2810 ($N-C\underline{H}_3$), 1310 (C-N), and 740cm^{-1} (aromatic 1,2-disubstitution), δ 7.2 - 6.5 (m, 4H, aromatic H), 3.0 - 2.6 (m, 7H, $N-CH_2$, $N-CH_3$ and benzylic CH_2) and 2.0 - 1.2 (m, 4H, CH_2-CH_2), G.C.$^{B}_{100}$° one peak.

Vinyloxymethylenebenzene (95)

The method described by Burgstahler et.al.[90] was used to prepare vinyloxymethylenebenzene as a colourless liquid, b.p. 85-87°/21mm (lit.[90] b.p. 85-87°/21mm), ν_{max} 3130 ($CH_2=C\underline{H}-O$), 3080 ($C\underline{H}_2=CH$), 1640 (olefinic C=C), 1200 (C-O), 990 and 905 ($CH_2=CH$), 735 and 695cm^{-1} (aromatic mono-substitution), δ 7.5 - 7.1 (m, 5H, aromatic H), 6.50 (dd, 1H, J=14.0 and 7.0 Hz, $O-C\underline{H}=CH_2$), 4.70 (s, 2H, CH_2-O), 4.20 (dd, 1H, J=14.0 and 2.0 Hz, ) and 4.00 (dd, 1H, J= 7.0 and 2.0 Hz, ), G.C.$^{B}_{100}$° one peak.

o-Iodobenzyl bromide

The procedure described by Bacon and Lindsay[134] was used

to prepare o-iodobenzyl bromide as a colourless crystalline solid, m.p. 55° (lit.[134] m.p. 55.5°).

o-Iodobenzyl acetate

o-Iodobenzyl bromide was solvolised[134] in a solution of sodium acetate in glacial acetic acid to give, after distillation under reduced pressure, o-iodobenzyl acetate as a colourless liquid (99%), b.p. 98-100°/0.5mm (lit.[134] b.p. 92°/0.4mm), ν_{max} 1735 (ester C=O), 1240 (ester C-O) and 755cm^{-1} (aromatic 1,2-disubstitution), δ 7.9 - 6.8 (m, 4H, aromatic H), 5.10 (s, 2H, O-CH_2) and 2.10 (s, 3H, O=C-CH_3).

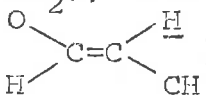
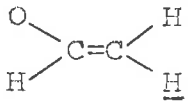
o-Iodobenzyl alcohol

The alkaline hydrolysis[134] of o-iodobenzyl acetate gave, on recrystallisation from hexane, o-iodobenzyl alcohol as a colourless crystalline solid (88%), m.p. 90° (lit.[134] m.p. 91°).

o-Vinyloxymethyleneiodobenzene (90)

The method for the preparation of vinyloxymethylene-benzene[90] was slightly modified in the following way:-

Mercuric acetate (0.2g) was added to a solution of o-iodobenzyl alcohol (4.68g) in ethyl vinyl ether (20ml) and the mixture was heated under reflux for 11 hr. A further portion of nercuric acetate (0.2g) was then added and heating under reflux was continued for a further 10 hr. The reaction mixture was then cooled to room temperature,

extracted with 10% aqueous potassium carbonate solution (2 x 20ml), dried (K_2CO_3) and concentrated under reduced pressure. The residue was diluted with pentane (25ml) and the solid o-iodobenzyl alcohol (0.80g) which precipitated, was removed by filtration. The filtrate was concentrated under reduced pressure and the residue was chromatographed on basic alumina with pentane as the eluant. The eluate was concentrated and distilled under reduced pressure to give o-vinyloxymethyleneiodobenzene as a colourless liquid (3.35g, 78%), b.p. 82-83°/0.8mm, (Found: C, 41.5; H, 3.4; I, 48.4. C_9H_9IO requires C, 41.6; H, 3.5; I, 48.8%), ν_{max} 3120 (CH_2=C<u>H</u>-O), 3070 ($C\underline{H}_2$=CH), 1640 (olefinic C=C), 1200 (C-O), 990 and 890 (CH_2=CH) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.9 - 6.8 (m, 4H, aromatic H), 6.55 (dd, 1H, J=14.0 and 7.0 Hz, O-C<u>H</u>=CH_2), 4.70 (s, 2H, CH_2-O), 4.30 (dd, 1H, J=14.0 and 2.0 Hz, ) and 4.10 (dd, 1H, J= 7.0 and 2.0 Hz, ), m/e 260, G.C.$_{120^o}^{B}$ one peak.

o-Acetylbenzoic acid

The method described by Yale[135] was used to prepare o-acetylbenzoic acid as a colourless crystalline solid, m.p. 114-115° (lit.[135] m.p. 114-115°).

∝-Methyl-o-xylene glycol

o-Acetylbenzoic acid was reduced with lithium aluminium hydride using a modification of the procedures of Pernot and Willemart[91] for the reduction of o-benzoylbenzoic acid to

∝-phenyl-o-xylene glycol and of Reiche and Schultz[92] for the reduction of 3-methylphthalide to the title compound:-

o-Acetylbenzoic acid (16.4g) was placed in a "Soxhlet" extractor fitted with an ether condenser carrying a drying tube. Lithium aluminium hydride (6.65g) in dry ether (310 ml) was stirred in a 500ml round bottom flask which was attached to the extractor by means of a ground glass joint. The flask was warmed gently until the boiling ether had begun to percolate through the contents of the extractor, then the source of heat was removed since the heat generated by the reaction was sufficient to maintain the contents of the flask at reflux. When the reaction had subsided the flask was warmed for 1 hr. in order to wash out the last traces of the acid from the extractor. The reaction mixture was then stirred at room temperature overnight. The stirred reaction mixture was then cooled to 0° and treated dropwise at 0° with water (7ml), 15% aqueous sodium hydroxide solution (7ml) and water (21ml). The reaction mixture was stirred at 0° for 30 min., then filtered. The filter cake was washed with several small portions of ether. The combined ether layers were dried (Na_2SO_4) and concentrated to give ∝-methyl-o-xylene glycol as a colourless crystalline solid (12.17g, 80%), m.p. 65-66° (lit.[92] m.p. 66-67°).

1-Methylphthalan (96)

∝-Methyl-o-xylene glycol was cyclodehydrated in the manner described by Reiche and Schultz[92] and after two distillations

under reduced pressure 1-methylphthalan was obtained as a colourless liquid, b.p. 84°/15mm (lit.[92] b.p. 82-83.5°/13mm), ν_{max} 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.4 - 7.0 (m, 4H, aromatic H), 5.5 - 4.9 (m, 3H, CH_2-O-CH) and 1.45 (d, 3H, J=6.0 Hz, C-CH_3), G.C.$^{B}_{100°}$ one peak.

Isochroman (97)

The method described by Maitte[136] was used to prepare isochroman as a colourless liquid (92%) b.p. 95-96°/13mm (lit.[137] b.p. 90°/12mm), ν_{max} 1110 (C-O) and 740cm^{-1} (aromatic 1,2-disubstitution), δ 7.2 - 6.7 (m, 4H, aromatic H), 4.65 (s, 2H, benzylic CH_2-O), 3.85 (t, 2H, J=5.5 Hz, O-CH_2) and 2.75 (t, 2H, J=5.5 Hz, benzylic CH_2), G.C.$^{B}_{120°}$ one peak.

Allyloxymethylenebenzene (98)

The method of Hauser and Kantor[93] was modified by adding sodium allyloxide to benzyl bromide, rather than the other way around as the authors suggest. The reaction mixture was worked-up as described[93], giving after distillation under reduced pressure allyloxymethylenebenzene as a colourless liquid (81%), b.p. 87-90°/12mm (lit.[93] b.p. 87-90°/12mm), ν_{max} 3080 and 3040 (CH_2=CH), 1650 (olefinic C=C), 1090 (C-O), 985 and 920 (CH_2=CH) 730 and 695cm^{-1} (aromatic monosubstitution), δ 7.4 - 6.9 (m, 5H, aromatic H), 6.2 - 5.5 (m, 1H, C<u>H</u>=CH_2), 5.4 - 4.9 (m, 2H, CH=C<u>H</u>$_2$), 4.45 (s, 2H, benzylic CH_2-O) and 4.0 - 3.7 (m, 2H, allylic CH_2-O), G.C.$^{B}_{100°}$ one peak.

o-Allyloxymethyleneiodobenzene (91)

This preparation was carried out by the treatment of o-iodobenzyl bromide with sodium allyloxide in the same manner as described above for compound (98). Distillation of the crude product under reduced pressure gave o-allyloxymethyleneiodobenzene as a colourless liquid (71%) b.p. 116-118°/3.6mm, (Found: C, 43.9; H, 4.2; I, 46.5. $C_{10}H_{11}IO$ requires C, 43.8; H, 4.1; I, 46.3%), ν_{max} 3070 and 3020 (CH_2=CH), 1085 (C-O), 985 and 920 (CH_2=CH) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.8 - 6.7 (m, 4H, aromatic H), 6.3 - 5.6 (m, 1H, C<u>H</u>=CH_2), 5.5 - 5.0 (m, 2H, CH=C<u>H</u>$_2$), 4.40 (s, 2H, benzylic CH_2-O) and 4.2 - 3.9 (m, 2H, allylic CH_2-O), m/e 274, G.C.$^{B}_{120}$° one peak.

2-Phenyl-1-propanol

Hydroboration-oxidation of α-methylstyrene as described by Brown and Zweifel[138] gave 2-phenyl-1-propanol as a colourless liquid, b.p. 107-109°/12mm (lit.[138] b.p. 114°/14mm).

4-Methylisochroman (99)

Chloromethylation-cyclodehydrohalogenation of 2-phenyl-1-propanol as described by Maitte[139] was used to prepare 4-methylisochroman which, after two distillations under reduced pressure, was obtained as a colourless liquid (85%), b.p. 100°/15mm (lit.[139] b.p. 101°/14mm), ν_{max} 1100 (C-O) and 740cm^{-1} (aromatic 1,2-disubstitution), δ 7.2 - 6.6 (m, 4H, aromatic

H), 4.65 (s, 2H, benzylic CH_2-O), 4.0 - 3.3 (m, 2H, CH_2-O), 3.1 - 2.4 (m, 1H, benzylic CH) and 1.25 (d, 3H, J=7 Hz, CH_3), G.C.$^{B}_{120^o}$ one peak.

3-Phenyl-1-propanol

Cinnamaldehyde was reduced with lithium aluminium hydride according to the directions of Nystrom and Brown[140] to give 3-phenyl-1-propanol as a colourless liquid b.p. 124-125°/14mm (lit.[141] b.p. 121-122°/14mm).

Chloromethyl (3-phenylpropyl) ether

3-Phenyl-1-propanol was chloromethylated, as described by Reiche and Gross[94], to give chloromethyl (3-phenylpropyl) ether as a colourless liquid, b.p. 130-132°/13mm (lit.[94] b.p. 122.5-123.5°/9mm), δ 7.3 - 6.9 (m, 5H, aromatic H), 5.40 (s, 2H, Cl-CH_2-O), 3.60 (t, 2H, J=6.0 Hz, O-CH_2), 2.9 - 2.5 (m, 2H, benzylic CH_2) and 2.2 - 1.6 (m, 2H, CH_2).

Homoisochroman (100)

Chloromethyl (3-phenylpropyl) ether was cyclodehydrohalogenated with anhydrous aluminium chloride using the method described by Reiche and Gross[94] with the slight modification methylene chloride instead of carbon disulphide was used as solvent. Distillation of the crude product under reduced pressure gave homoisochroman as a colourless liquid (72%), b.p. 110-112°/13mm (lit.[94] b.p. 103.5-104.5°/8.5mm), ν_{max} 1085 (C-O) and 750cm^{-1} (aromatic 1,2-disubstitution), δ 7.2 - 6.8 (m, 4H, aromatic H), 4.50 (s, 2H,

benzylic CH_2-O), 4.0 - 3.8 (m, 2H, O-CH_2), 3.1 - 2.8 (m, 2H, benzylic CH_2) and 2.0 - 1.5 (m, 2H, CH_2), G.C.$^{B}_{110}$° one peak.

(3-Butenyl)benzene(92e)

The method desctibed by Hurd and Bollman[142] was used to prepare (3-butenyl)benzene as a colourless liquid, b.p. 175-178° (lit.[142] 175-178°), δ 7.4 - 6.9 (m, 5H, aromatic H), 6.1 - 5.5 (m, 1H, C<u>H</u>=CH_2), 5.2 - 4.7 (m, 2H, CH=C<u>H</u>$_2$) and 2.9 - 2.0 (m, 4H, CH_2-CH_2), G.C.$^{A}_{110}$° one peak.

<u>o</u>-(3-Butenyl)chlorobenzene

A method similar to the one described by Bott <u>et.al.</u>[143] was used:-

<u>o</u>-Chlorobenzyl bromide (25.75g) in dry ether (100ml) was added dropwise during 1lhr. to a stirred suspension of magnesium turnings (3.04g) in dry ether (10ml) under an atmosphere of pure nitrogen. When the addition was complete the reaction mixture was stirred at room temperature for 1 hr., then allyl bromide (15.13g) in dry ether (50ml) was added dropwise and the resulting mixture stirred for 2 hr. The contents of the flask were then poured into dilute sulphuric acid, the ether layer separated, and the aqueous layer extracted with ether. The combined ether layers were washed with water, saturated aqueous sodium bicarbonate solution and saturated brine, dried ($MgSO_4$) and concentrated. The residue was distilled under reduced pressure to give

o-(3-butenyl)chlorobenzene as a colourless liquid (16.05g, 77%), b.p. 100-102°/22mm (lit.[143] b.p. 86-88°/10mm), ν_{max} 3090 and 3020 (CH_2=CH), 1645 (olefinic C=C), 990 and 910 (CH_2=CH) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.4 - 6.9 (m, 4H, aromatic H), 6.2 - 5.4 (m, 1H, C<u>H</u>=CH_2), 5.2 - 4.7 (m, 2H, CH=C<u>H</u>$_2$), 3.0 - 2.6 (m, 2H, benzylic CH_2) and 2.6 - 2.1 (m, 2H, allylic CH_2), G.C.$^{A}_{120°}$ one peak.

<u>Diiodoacetylene</u>

The method of Dehn[144] was used to prepare diiodoacetylene as a yellowish crystalline solid m.p. 81° (lit.[144] m.p. 81°).

<u>o-(3-Butenyl)iodobenzene</u> (88c)

The method of converting aryl chlorides or bromides to aryl iodides as described by Franzen[95] was adapted:-

A stirred mixture of o-(3-butenyl)chlorobenzene (4.18g, 0.025mole) and magnesium turnings (0.65g, 0.025mole) in dry tetrahydrofuran (10ml) was boiled under reflux under an atmosphere of pure nitrogen until all the magnesium had reacted. The reaction mixture was cooled to 0° and a solution of diiodoacetylene (3.475g, 0.0125mole) in dry ether was added with stirring and the resulting mixture was stirred at 0° for 15 min. The contents of the flask were then poured into dilute sulphuric acid and ether (50ml) was added. The ether layer was separated, and the aqueous layer extracted with ether (2 x 50ml). The combined ether layers were washed with water, saturated aqueous sodium bicarbonate

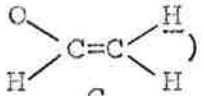
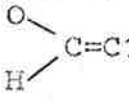
solution and saturated brine, dried ($MgSO_4$) and concentrated. The residue was distilled under reduced pressure to give o-(3-butenyl)iodobenzene as a colourless liquid (4.08g, 63%), b.p. 130-132°/19mm, (Found: C, 46.5; H, 4.3. $C_{10}H_{11}I$ requires C, 46.5; H, 4.3%), ν_{max} 3080 and 3020 (CH_2=CH), 1645 (olefinic C=C), 990 and 910 (CH_2=CH) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.9 - 6.6 (m, 4H, aromatic H), 6.2 - 5.5 (m, 1H, C<u>H</u>=CH_2), 5.2 - 4.7 (m, 2H, CH=C<u>H</u>$_2$), 2.9 - 2.6 (m, 2H, benzylic CH_2) and 2.6 - 2.1 (m, 2H, allylic CH_2), m/e 258, G.C.$^{B}_{130°}$ one peak.

1-Methylindan (93e)

The reaction sequence of Schaap and Pines[145] was used to prepare 1-methylindan as a colourless liquid, b.p. 192° (lit.[145] b.p. 190°/748mm), δ 7.4 - 6.8 (m, 4H, aromatic H), 3.5 - 3.2 (m, 1H, benzylic CH), 3.1 - 1.7 (m, 4H, CH_2-CH_2) and 1.30 (d, 3H, J=6 Hz, CH_3), G.C.$^{A}_{110°}$ one peak.

Vinyloxybenzene (92f)

2-Phenoxyethanol-p-toluene sulphonate (8.76g, 0.030mole) was added portionwise with stirring to a solution of potassium t-butoxide (3.70g, 0.033mole) in dry dimethyl formamide (50ml) kept at 0° under an atmosphere of pure nitrogen. The mixture was stirred at 0° for 2 hr., then at room temperature for 8 hr. The reaction mixture was then filtered, diluted with water (200ml) and extracted with pentane (3 x 100ml). The combined pentane extracts

were washed with 10% aqueous sodium hydroxide solution (2 x 100ml) and water (2 x 100ml), dried (Na_2SO_4) and concentrated. The residue was distilled under reduced pressure to give vinyloxybenzene as a colourless liquid (1.38g, 38%), b.p. 80°/60mm (lit.[146] b.p. 76.5-77.5°/50mm), ν_{max} 3100 (O-C<u>H</u>=CH_2), 3070 (CH=C<u>H</u>$_2$), 1645 (vinylic C=C), 1230 (C-O), 955 and 845 (CH=CH_2), 750 and 685cm^{-1} (aromatic monosubstitution), δ 7.4 - 6.7 (m, 5H, aromatic H), 6.55 (dd, 1H, J=13.5 and 6.0 Hz, O-C<u>H</u>=CH_2), 4.60 (dd, 1H, J=13.5 and 1.5 Hz, ) and 4.30 (dd, 1H, J=6.0 and 1.5 Hz, ), G.C.$_{120°}$ one major peak (99%) and one small peak (1%).

2'-Bromoethyl o-iodophenyl ether

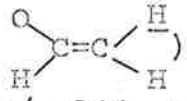
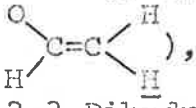
A mixture of o-iodophenol (4.40g, 0.02mole) and 1,2-dibromoethane (20.0g, 0.1mole) in water (50ml) was boiled under reflux with stirring, and a solution of sodium hydroxide (0.80g, 0.02mole) in water (15ml) was added dropwise during 50 min. The mixture was boiled under reflux overnight, then cooled and extracted with ether (3 x 50ml). The combined ether layers were washed with 10% aqueous sodium hydroxide solution (3 x 100ml) and saturated brine, dried ($MgSO_4$) and concentrated. The residue was distilled under reduced pressure to give 2'-bromoethyl o-iodophenyl ether as a colourless liquid which solidified on standing (3.31g, 51%), b.p. 172-174°/13mm, m.p. 48-49° (lit.[147] b.p.

125-130°/1-2mm, m.p. 48-49°).

o-Vinyloxyiodobenzene (88d)

The method of dehydrohalogenation using ethyldicyclohexylamine as base according to Hunig and Kiessel[96] was adapted for this preparation:-

A mixture of 2'-bromoethyl o-iodophenyl ether (2.69g) and ethyldicyclohexylamine (2.55g) was heated at 170-180° for 5 hr., then cooled to room temperature and diluted with dry acetone. The precipitated amine hydrobromide was filtered off and the filtrate was diluted with saturated brine and extracted with ether (3 x 50ml). The combined ether layers were washed with 2N hydrochloric acid (2 x 100ml), water (100ml), 10% aqueous sodium hydroxide solution (2 x 100ml) and saturated brine, dried ($MgSO_4$) and concentrated to give a liquid (1.03g). The crude product was chromatographed on basic alumina with hexane-ether mixtures as the eluants. Concentration of the eluate gave a liquid (0.87g), G.C.$^{C}_{125}$o two peaks, of which one was identified as ethyldicyclohexylamine by spiking. The crude mixture was separated by preparative gas chromatography using a 5ft x $\frac{3}{8}$in. column of 30% S.E.30 on Chromosorb W support at 120° with 150ml/min. flowrate, giving after short path distillation o-vinyloxyiodobenzene as a colourless liquid (0.065g), δ 7.8 - 6.6 (m, 4H, aromatic H), 6.45 (dd, 1H, J=13.5 and 6.0 Hz, O-C<u>H</u>=CH_2), 4.65 (dd, 1H, J=13.5

and 1.5 Hz,  and 4.40 (dd, 1H, J=6.0 and 1.5 Hz, ), m/e 246, G.C.$^{C}_{125}$o one peak.

2,3-Dihydrobenzofuran (94f)

Benzofuran was reduced with sodium in ethanol, using the same procedure as described for 3-methylbenzofuran, to give after distillation under reduced pressure 2,3-dihydrobenzofuran as a colourless liquid (89%), b.p. 78°/12mm (lit.[116] b.p. 82-83°/19mm), ν_{max} 1230 (C-O) and 745cm^{-1} (aromatic 1,2-disubstitution), δ 7.2 - 6.4 (m, 4H, aromatic H), 4.35 (t, 2H, J=8.5 Hz, O-CH_2) and 3.00 (t, 2H, J=8.5 Hz, benzylic CH_2), G.C.$^{C}_{120}$o one peak.

6.3. SYNTHESES OF AMINES AND OF THEIR RESPECTIVE DIAZONIUM SALTS FOR ELECTRON PARAMAGNETIC RESONANCE STUDIES

o-Allyloxyacetanilide

The alkylation of o-acetamidophenol with allyl bromide as described by Tiffany[97] gave o-allyloxyacetanilide as colourless plates (86%), m.p. 50-52° (lit.[97] m.p. 50-51°).

o-Allyloxyaniline (83d)

Hydrolysis[97] of the above acetanilide gave o-allyloxyaniline, after distillation under reduced pressure, as a colourless liquid (78%), b.p. 76°/0.5mm (lit.[97] b.p. 84-85°/0.6mm), ν_{max} 3470, 3375 and 3200 (NH_2), 3065 and 3035 ($CH=CH_2$), 1640 (olefinic C=C), 1225 (C-O), 995 and 926 ($CH=CH_2$) and 746cm^{-1} (aromatic 1,2-disubstitution), δ 6.7 - 6.4 (m, 4H, aromatic H), 6.3 - 5.7 (m, 1H, $CH=CH_2$), 5.6 - 5.1 (m, 2H, $CH=CH_2$), 4.6 - 4.4 (m, 2H, $O-CH_2$) and 3.57 (s, 2H, NH_2), G.C.$^{B}_{120°}$ one peak.

o-Allyloxynitrobenzene

Allyl bromide (100g, 0.82mole) was added dropwise to a stirred mixture of o-nitrophenol (105g, 0.75mole) and anhydrous potassium carbonate (116g, 0.84mole) in acetone (200ml). The reaction mixture was then boiled under reflux with stirring until the red colour of the o-nitrophenolate anion had disappeared (20 hr.). The reaction mixture was then diluted in water (1 l.) and extracted with chloroform (3 x

250ml). The combined chloroform layers were washed thoroughly with saturated aqueous sodium bicarbonate solution and water, dried ($MgSO_4$) and concentrated. The residue was distilled under reduced pressure to give o-allyloxynitrobenzene as a yellow liquid (123g, 95%), b.p. 116-117°/0.7mm (lit.[148] b.p. 123-125°/3mm), ν_{max} 3075 and 3010 ($CH=CH_2$), 1650 (olefinic C=C), 1520 and 1335 (NO_2), 980 and 920 ($CH=CH_2$), 845 (C-N) and 735cm^{-1} (aromatic 1,2-disubstitution), δ 7.8 - 6.8 (m, 4H, aromatic H), 6.1 - 5.7 (m, 1H, $CH=CH_2$), 5.6 - 5.1 (m, 2H, $CH=CH_2$) and 4.8 - 4.5 (m, 2H, $O-CH_2$).

o-Allyloxyaniline (83d)

The procedure of Hodgson and Smith[100] for the reduction of aromatic nitro-compounds was adapted:-

Stannous chloride dihydrate (13.54g) in ethanol (20ml) was added dropwise to a stirred solution of o-allyloxynitrobenzene (3.58g) in concentrated hydrochloric acid (20ml) and ethanol (10ml) whilst keeping the temperature of the reaction mixture below 30°. The reaction mixture was stirred at room temperature for 18 hr., then diluted with water (100ml) and washed with small portions of ether until the ethereal extract was no longer yellow. The aqueous layer was then made alkaline (pH 10) by the dropwise addition of 20% aqueous sodium hydroxide solution and extracted several times with chloroform. The combined chloroform layers were washed with water, dried ($MgSO_4$) and concentrated

under reduced pressure. The residue was distilled under reduced pressure to give o-allyloxyaniline as a colourless liquid (2.27g, 84%), b.p. 118-119°/0.8mm (lit.[97] b.p. 84-85°/0.6mm), G.C.$^{B}_{120}$° one peak. The spectral characteristics and the G.C. retention time were identical with those of o-allyloxyaniline obtained by the procedure described above.

o-(2-Methylallyloxy)nitrobenzene

A stirred mixture of o-nitrophenol (35g), 2-methylallyl chloride (30g), sodium carbonate (15.9g) and sodium bromide (5g) in acetone (100ml) was boiled under reflux for 2 days. The reaction mixture was worked-up as in the case of o-allyloxynitrobenzene. Distillation under reduced pressure gave o-(2-methylallyloxy)nitrobenzene as a yellowish liquid (16.40g, 34%), b.p. 108°/0.1mm (lit.[149] 86-107°/0.1mm), δ 7.8 - 6.8 (m, 4H, aromatic H), 5.2 - 4.8 (m, 2H, C=CH_2), 4.50 (s, 2H, O-CH_2), and 1.83 (s, 3H, CH_3), m/e 193.

o-(2-Methylallyloxy)aniline (83e)

The reduction of o-(2-methylallyloxy)nitrobenzene, in the same manner as described for o-allyloxynitrobenzene, gave o-(2-methylallyloxy)aniline as a colourless liquid (77%), b.p. 96°/1.4mm, (Found: C, 73.4; H, 8.1; N, 8.3. $C_{10}H_{13}NO$ requires C, 73.6; H, 8.0; N, 8.6%), δ 6.8 - 6.3 (m, 4H, aromatic H), 5.4 - 4.9 (m, 2H, C=CH_2), 4.33 (s, 2H, O-CH_2) and 1.80 (s, 3H, CH_3), m/e 163, G.C.$^{B}_{120}$° one peak.

o-(3-Butenyloxy)nitrobenzene

A stirred mixture of o-nitrophenol (7g), 4-bromo-1-butene (7.43g) and sodium carbonate (3.2g)in water (20ml) was boiled under reflux for 2 days. The reaction mixture was then worked-up as described previously for o-allyloxynitrobenzene. Distillation of the crude product under reduced pressure gave o-(3-butenyloxy)nitrobenzene as a yellowish liquid (7.80g, 81%), b.p. 102°/0.07mm, (Found: C, 62.5; H, 5.5; N, 7.5. $C_{10}H_{11}NO_3$ requires C, 62.2; H, 5.7; N,7.3%), δ 7.8 - 6.8 (m, 4H, aromatic H), 6.2 - 5.6 (m, 1H, $C\underline{H}=CH_2$), 5.4 - 4.9 (m, 2H, $CH=C\underline{H}_2$), 4.10 (t, 2H, J=6.5 Hz, $O-C\underline{H}_2$) and 2.8 - 2.3 (m, 2H, allylic CH_2), m/e 193.

o-(3-Butenyloxy)aniline (83f)

The reduction of o-(3-butenyloxy)nitrobenzene, as described for o-allyloxynitrobenzene, gave after distillation under reduced pressure o-(3-butenyloxy)aniline as a colourless liquid (75%), b.p. 96-98°/0.8mm, (Found: C, 73.3; H, 8.0; N, 8.5. $C_{10}H_{13}NO$ requires C, 73.6; H, 8.0; N, 8.6%), δ 6.8 - 6.3 (m, 4H, aromatic H), 6.0 - 5.5 (m, 1H, $C\underline{H}=CH_2$), 5.3 - 4.8 (m, 2H, $CH=C\underline{H}_2$), 3.90 (t, 2H, J=6.5 Hz, $O-C\underline{H}_2$), 3.60 (s, 2H, NH_2) and 2.7 - 2.1 (m, 2H, allylic CH_2), m/e 163, G.C.$^{B}_{120}$° one peak.

o-(3-Butenyl)benzoic acid (107a)

The alkylation of toluic acid referred to in a note by

Creger[105] was adapted in the following manner:-

A solution of dry allyl bromide (30.25, 0.25mole) in dry tetrahydrofuran (25ml) was thoroughly degassed on a vacuum line and sealed into an ampoule (fitted with a "break-seal") under high vacuum. A 1 l. flask was fitted with a thermometer pocket (sealed into the flask), a ground glass jointed neck and a tube fitted with a ground glass needle valve (the "needle" of the valve consisted of a piece of glass tubing drawn to a point at one end with a piece of mild steel sealed into it). The ampoule of the allyl bromide solution and an ampoule of butyllithium in cyclo-hexane (117.2ml, 0.193mole) were sealed to the upper portion of the needle valve with their "break-seals" pointing downwards. Two small pieces of mild steel were also included in the tube below the "break-seals". Lithium o-toluate (27.26g, 0.193mole) and a magnetic stirrer bar were placed in the flask which was attached to and evacuated on a high vacuum line. A solution of dry diisopropylamine (28ml, 0.2mole) in dry tetrahydrofuran (200ml) was thoroughly degassed on the vacuum line and distilled into the reaction flask which was cooled in liquid nitrogen. The reaction flask, whilst still under high vacuum, was sealed, and immersed in an ice bath on a magnetic stirrer. The break-seal of the ampoule of butyllithium was then broken. The addition of butyllithium to the stirred reaction mixture was regulated with the needle valve, which was

adjusted by means of a powerful permanent magnet, to keep the reaction temperature between 0 and 5°. The mixture was then stirred at 0° for 20 min. The break-seal of the allyl bromide solution was then broken and its addition was regulated as above whilst keeping the stirred reaction mixture between 0 and 15°. The flask was then opened and the solvent removed under reduced pressure on a rotary film evaporator. The residue was treated with water (250ml) then with concentrated hydrochloric acid solution (30ml). This mixture was extracted with ether (3 x 150ml). The combined ether layers were washed with saturated brine, dried ($MgSO_4$) and concentrated to give a colourless solid (33.78g), δ ($CHCl_3$) 11.70 (s, 1H, CO_2H), 8.2 - 7.0 (m, 4H, aromatic H), 6.2 - 5.4 (m, 0.5H, $C\underline{H}=CH_2$), 5.2 - 4.7 (m, 1.0H, $CH=CH_2$), 3.4 - 2.9 (m, 1.0H, benzylic CH_2) and 2.9 - 1.9 (m, 3.2H, CH_2 and CH_3). This spectrum indicates the presence of toluic acid in the required o-(3-butenyl)-benzoic acid. Recrystallization from pentane did not separate the toluic acid from the mixture. The above mixture (approx. 1:1) was used in the subsequent step, without purification.

o-(3-Butenyl)benzoyl chloride (107c)

To oxalyl chloride (8.2g) in dry benzene (160ml) was added with stirring the above mixture of acids (6.0g) and dry pyridine (3.16g) in dry benzene (30ml) during 30 min.

The resulting mixture was stirred at room temperature for 1 hr., then the pyridinium hydrochloride precipitate was removed by filtration. The filtrate was concentrated under reduced pressure to give a viscous liquid (7.67g) which was used in the next step without purification.

o-(3-Butenyl)benzamide (107d)

The above mixture of acid chlorides (7.0g) was added dropwise to concentrated ammonium hydroxide solution (24ml) with vigorous shaking and cooling in an ice bath. The mixture was shaken at 0° for a further 15 min. then the mixture of solid amides was collected by filtration, washed with water, air dried and used in the next step without purification.

o-(3-Butenyl)aniline (107e)

The above mixture of amides (4.37g) was added to a solution of sodium hypochlorite (0.025mole) at 0°. The resulting mixture was placed in a water bath at room temperature. The bath was then heated slowly until the temperature of the reaction mixture reached 70°. The mixture was kept at 70° for 1 hr., then a solution of sodium hydroxide (10g) in water (10ml) was added. The reaction mixture was then warmed to 80° and kept at that temperature for 1 hr. The reaction mixture was then cooled to 0° and treated with concentrated hydrochloric acid until the solution was acidic (pH 2), then extracted with chloroform

several times. The aqueous layer was adjusted to pH 10 by the addition of 10% sodium hydroxide solution and extracted with ether. The ether layer was washed with saturated brine, dried (Na_2SO_4) and concentrated to give a dark oil (0.22g), δ 7.2 - 6.0 (m, 4H, aromatic H), 6.0 - 5.4 (m, 0.75H, $C\underline{H}=CH_2$), 5.2 - 4.7 (m, 1.5H, $CH=C\underline{H}_2$), 3.40 (s, 2H, NH_2), and 2.7 - 1.8 (m, 4H, CH_2-CH_2 and CH_3). This spectrum indicates the presence of some of the required o-(3-butenyl)aniline along with some o-toluidine. The quantity of the required amine was insufficient for the proposed e.p.r. studies.

o-(4-Pentenyl)benzoic acid (107b)

This acid was obtained by the alkylation of lithium toluate with 4-bromo-1-butene in an identical manner to that described for o-(3-butenyl)benzoic acid. Unfortunately the required acid was contaminated by toluic acid, which could not be separated from it by recrystallisation from pentane. The n.m.r. spectrum of the above mixture (approx. 1:1) showed:- δ 12.23 (s, 1H, CO_2H), 8.2 - 7.0 (m, 4H, aromatic H), 6.2 - 5.6 (m, 0.5H, $C\underline{H}=CH_2$), 5.3 - 4.7 (m, 1H, $CH=C\underline{H}_2$), 3.2 - 2.8 (t, 1H, J=7 Hz, benzylic CH_2), 2.67 (s, 1.6H, CH_3) and 2.4 - 1.5 (m, 2.0H, CH_2-CH_2).

o-Allyloxybenzenediazonium borofluoride (83a)

This method was used for the preparation of all of the arenediazonium borofluorides:-

Sodium nitrite (4.38g) in water (9ml) was added dropwise to a stirred solution of o-allyloxyaniline (9.30g) in 21% fluoroboric acid (54ml) whilst the temperature of the reaction mixture was maintained at 10°. The reaction mixture was then cooled to -20°. The precipitated product was collected by filtration, washed with cold 5% fluoroboric acid (20ml), air dried at room temperature, and then washed with ether until it was almost colourless. The solid was then dissolved in dry acetone and reprecipitated by the addition of dry ether. The precipitate was filtered off and dried under vacuum. The required diazonium borofluoride was obtained as a colourless powder (12.70g, 76%), ν_{max} (nujol) ~ 3100 ($CH=CH_2$), 2275 (N_2^+), 1055 and 1035 (BF_4^-), 980 and 925 ($CH=CH_2$) and 760cm^{-1} (aromatic 1,2-disubstitution).

o-(2-Methylallyloxy)benzenediazonium borofluoride (83b)

The required diazonium borofluoride was obtained from o-(2-methylallyloxy)aniline, by the standard procedure described above, as a colourless powder (80%), ν_{max} (nujol) ~ 3100 ($CH=CH_2$), 2275 (N_2^+), 1055 and 1035 (BF_4^-), 975 and 920 ($CH=CH_2$) and 755cm^{-1} (aromatic 1,2-disubstitution).

o-(3-Butenyloxy)benzenediazonium borofluoride (83c)

The required diazonium borofluoride was obtained from o-(3-butenyloxy)aniline, by the standard method described above, as a colourless powder (60%), ν_{max} (nujol) ~ 3100 ($CH=CH_2$), 2275 (N_2^+), 1055 and 1035 (BF_4^-), 980 and 930 ($CH=CH_2$)

and 760cm^{-1} (aromatic 1,2-disubstitution).

o-Methoxybenzenediazonium borofluoride

The required diazonium borofluoride was prepared from o-methoxyaniline, by the method described above, as a colourless powder (80%).

6.4. RECORDING OF THE ELECTRON PARAMAGNETIC RESONANCE SPECTRA

A Varian E9 e.p.r. spectrometer with 100 KHz modulation and an X-band Klystron was used in conjunction with a 3-way quartz mixing cell[79]. Splitting constants and g-factors were measured by comparison with an aqueous solution of Fremy's salt.

General procedure

Three reservoirs were charged with the following solutions:-

(i) 0.008M-titanium (III) chloride, 0.016M-disodium ethylenediaminetetra-acetate and sufficient aqueous ammonium hydroxide solution for the required pH (7-9).

(ii) 0.008M-arenediazonium borofluoride containing ice and one drop concentrated sulphuric acid.

(iii) Water (2 l.).

The flows from the above reservoirs were regulated to obtain the maximum intensity of absorption. The water in reservoir (iii) was used to speed-up the flow through the cell in order to prevent any blockages that may occur. For competitive experiments, ethanol or maleic acid (2g/l.) or trimesic acid (1g/l.) were added to the solution in reservoir (i). The solutions in all reservoirs were deaerated by bubbling a brisk stream of high-purity nitrogen through them.

6.5. REDUCTIONS OF o-ALLYLOXYBENZENEDIAZONIUM BORO-FLUORIDE WITH VARIOUS REDUCING REAGENTS

The following experiments were carried out:-

(i) A solution of the diazonium salt (1.00g) in acetone (50ml) and distilled water (10ml) was placed in a 2-necked flask fitted with a pressure equalized dropping-funnel, a thermometer, a magnetic stirrer bar and a nitrogen inlet. A solution of titanous chloride 2.25% w/v in water (23.5ml) was added dropwise with stirring whilst the reaction mixture was kept at -10° under an atmosphere of pure nitrogen. The reaction mixture was then stirred at -10° for 5 min., at 0° for 75 min. and at 10° for 15 min. The mixture was then poured into water (200ml) and extracted with methylene chloride several times. The extracts were washed with water, dried ($MgSO_4$) and concentrated. The residue was subjected to short path distillation giving an oil (0.26g). Analysis of this oil by quantitative gas chromatography using an internal standard indicated that only a very small amount of low molecular weight product was present in the oil.

(ii) The apparatus used was the same as in (i). A solution of titanous chloride 2.25% w/v in water (23.5ml) was added dropwise during 15 min. with vigorous stirring to a solution of the diazonium salt (1.00g) in water (30ml) and cyclohexane (30ml) whilst keeping the reaction mixture

at 10-15° under an atmosphere of pure nitrogen. The stirring was continued at 10° for 15 min. then at room temperature overnight. The layers were separated and the aqueous layer was extracted with cyclohexane. The combined organic layers were washed with water, dried (Na_2SO_4) and the solvent removed by fractionation giving an oil (0.44g). Analysis by gas chromatography as in (i) indicated that only very small amount of low molecular weight products was present.

(iii) The apparatus used was the same as in (i). A solution of the diazonium salt (1.00g) in ice water (150ml) was added dropwise with stirring during 25 min. to a solution of titanous chloride 1% w/v in water (53.5ml) and ethanol (5ml) whilst keeping the reaction mixture at 0° under an atmosphere of pure nitrogen. The resulting mixture was stirred at 0° for a further 30 min., then worked-up and analysed as in (i). Only very small yield of low molecular weight products was obtained.

(iv) In this reaction, chromous sulphate was used as the reducing agent. The reduction was carried out as in (i). Once again only a very poor conversion to low molecular weight products was realised.

(v) Potassium ferrocyanide was used as the reducing agent in this reaction which was conducted as the reduction in (iii). A very low yield of volatile products was obtained.

(vi) One reservoir was filled with a solution of disodium ethylenediaminetetra-acetic acid (24.0g) in water (500ml). Whilst the contents of the reservoir were being deaerated with a brisk stream of pure nitrogen an aqueous solution of titanous chloride 15% w/v (10ml) was added to it, followed by potassium carbonate (4.0g) and methanol (500ml). The other reservoir contained an ice cold solution of the diazonium salt in 1:1 methanol-water mixture (1 l.). The solutions in the two reservoirs were allowed to pass through a mixing chamber over a period of 15 min., and the effluent collected was allowed to stand at room temperature under an atmosphere of pure nitrogen overnight. The reaction mixture was then extracted 3 times with pentane and 3 times with ether. The combined pentane extracts were washed with saturated brine, dried ($MgSO_4$) and concentrated to yield an oil (0.712g). The combined ether extracts were washed with saturated brine, dried ($MgSO_4$) and concentrated to yield a tarry product (0.022g). Analysis of the major product by quantitative gas chromatography using an internal standard showed that allyloxybenzene (0.010g, 2%) and 3-methyl-2,3-dihydrobenzofuran (0.061g, 11%) were present. Chroman was not detected amongst the products.

(vii) Three experiments were carried out using the technique described by Burnett and Takayama[82]:-

(a) To a 2M solution of sodium methoxide in methanol (10ml)

under an atmosphere of pure nitrogen the diazonium salt (0.248g) was added with stirring. The mixture was then heated under reflux for 5 min., then cooled in an ice bath and poured into water (20ml). This mixture was extracted with ether (3 x 20ml). The combined ethereal extracts were washed with water and saturated brine, dried ($MgSO_4$) and concentrated. The residue was analysed by quantitative gas chromatography using an internal standard. The estimated yields of 3-methyl-2,3-dihydrobenzofuran and allyloxybenzene were 28% and 5% respectively.

(b) Experiment was carried out as in (a) with the exception that the diazonium salt was added at 0°. Estimated yields of 3-methyl-2,3-dihydrobenzofuran and allyloxybenzene were 31% and 5% respectively.

(c) This experiment in a 2M solution of sodium isopropoxide in isopropanol (10ml) was conducted as in (a). The estimated yields of 3-methyl-2,3-dihydrobenzofuran and allyloxybenzene were 1.5% and 7% respectively.

Chroman was not detected in any of the reduction products in (a), (b) and (c).

6.6. REDUCTIONS OF ARYL IODIDES WITH TRI-n-BUTYL-STANNANE

Tri-n-butylstannane (preparation)

The reduction of tri-n-butyltin chloride with lithium aluminium hydride, using the procedure described by Kuivila and Beumel[150], gave the required stannane. The stannane was flash distilled under high vacuum, sealed into small ampoules whilst still under vacuum and stored in the dark at 0°.

Purification of benzene

The benzene used in these reductions was reagent grade and was distilled from calcium hydride.

REDUCTIONS:-

(i) o-Allyloxyiodobenzene (88a)

(a) o-Allyloxyiodobenzene (0.6515g) was made up to 5ml with benzene and the solution was weighed. Azobisisobutyronitrile (A.I.B.N.) (4.5mg) was added to this solution. Weighed 0.5ml aliquots of this solution were pipetted into ten reaction tubes.

(b) Tri-n-butylstannane (2.4265g) was made up to 10ml in benzene and the solution weighed.

(c) Reaction mixtures:-

The following weighed aliquots of the stannane solution were placed into the reaction tubes containing the

aryl iodide solutions:-

2 x 0.3ml, 2 x 0.6ml, 2 x 1.2ml and 2 x 2.4ml.

The eight reaction mixtures and the two blanks were each made up to 2.9ml by addition of the appropriate quantity of benzene, then sealed under vacuum (0.05mm) whilst frozen in an ethanol-dry ice bath.

(d) Reduction conditions:-

The tubes were heated in the dark at 127° for 24 hr.

(e) Work-up procedure:-

When cool the reaction tubes were opened and the reaction mixtures quenched by the addition of weighed 1.0ml aliquots of carbon tetrachloride containing a known amount of internal standard.

(f) Gas chromatographic analysis:-

Each reaction mixture was analysed by gas chromatography (column A at 130°). The area under each peak was determined by means of a printing integrator. Calibration graphs were obtained by analysing, under identical conditions, accurately weighed mixtures of the internal standard and the expected products:- allyloxybenzene (92a), 3-methyl-2,3-dihydrobenzofuran (93a) and chroman (94a).

For table of results see following page.

(g) Results:-

Initial concn. of 88a (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92a (%)	Relative yield of 93a (%)	Relative yield of 94a (%)	Absolute yield of reduction* (%)
0.086	-	-	-	-	-
0.086	-	-	-	-	-
0.086	0.086	0	100	0	71
0.086	0.086	0	100	0	73
0.086	0.172	trace	100	0	quant.
0.086	0.172	trace	100	0	quant.
0.086	0.344	trace	100	0	quant.
0.086	0.344	trace	100	0	quant.
0.086	0.688	trace	100	0	quant.
0.086	0.688	trace	100	0	quant.

* Where yields are less than 100%, the starting material (88a) was detected in the reaction mixtures.

(ii) o-(3-Butenyloxy)iodobenzene (39a)

(a) o-(3-Butenyloxy)iodobenzene (0.6950g) in benzene (10ml) and A.I.B.N. (2mg).

(b) Tri-n-butylstannane (6.2002g) in benzene (25ml).

(c) Reaction mixtures:-

2 x [1.0ml of (a)], 2 x [1.0ml of (a) and 0.3ml of (b)], 2 x [1.0ml of (a) and 0.6ml of (b)], 2 x [1.0ml of (a) + 1.2ml of (b)] and 2 x [1.0ml of (a) + 2.4ml of (b)].

Each mixture was made up to 3.4ml with the appropriate amount of benzene, then sealed under vacuum (0.05mm) whilst frozen in an ethanol-dry ice bath.

(d) Reaction conditions:-

Temperature: 128°C, time 24hr.

(e) Work-up procedure:-

As in (i).

(f) Gas chromatographic analysis:-

Column B (initial temperature: 100° (5min.) then programmed to 130°). Calibration graphs obtained with mixtures of internal standard and (3-butenyloxy)-benzene (92b), 4-methylchroman (93b) and 2,3,4,5-tetrahydro-1-benzoxepin (94b).

For table of results see following page.

(g) Results:-

Initial concn. of 89a (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92b (%)	Relative yield of 93b (%)	Relative yield of 94b (%)	Absolute yield of reduction* (%)
0.082	-	-	-	-	-
0.081	-	-	-	-	-
0.082	0.074	13	87	0	50
0.082	0.074	15	85	0	53
0.081	0.149	19	81	0	88
0.081	0.150	20	80	0	86
0.082	0.298	25	75	0	96
0.082	0.299	25	75	0	96
0.081	0.595	38	62	0	99
0.082	0.596	37	63	0	98

* Where yields are less than 100%, starting material (89a) was detected in the reaction mixtures.

(iii) o-(N-Allyl-N-methylamino)iodobenzene (88b)

(a) N-Allyl-N-methylaminoiodobenzene (0.6850g) in benzene (10ml) and A.I.B.N. (2.5mg).

(b) Tri-n-butylstannane (2.4310g) in benzene (10ml).

(c) Reaction mixtures:-

As in (ii).

(d) Reaction conditions:-

Temperature: 130°, time 24 hr.

(e) Work-up procedure:-

As in (i).

(f) Gas chromatographic analysis:-

Column B (temperature 130°). Calibration graphs obtained with mixtures of internal standard, N-allyl-N-methylaminobenzene (92c), 1,3-dimethylindoline (93c) and N-methyl-1,2,3,4-tetrahydroquinoline (94c).

For table of results see following page.

(g) Results:-

Initial concn. of 88b (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92c (%)	Relative yield of 93c (%)	Relative yield of 94c (%)	Absolute yield of reduction* (%)
0.072	-	-	-	-	-
0.073	-	-	-	-	-
0.073	0.069	4	96	0	82
0.073	0.069	3	97	0	82
0.074	0.146	7	93	0	98
0.074	0.146	7	93	0	94
0.074	0.293	11	89	0	92
0.074	0.295	12	88	0	94
0.074	0.590	15	85	0	86
0.073	0.593	15	85	0	90

*Where yields are less than 100% starting material (88b) was detected in the reaction mixtures.

(iv) o-[N-(3-Butenyl)-N-methylamino]iodobenzene (89b)

(a) o-[N-(3-Butenyl)-N-methylamino]iodobenzene (0.7096g) in benzene (10ml) and A.I.B.N. (3.9mg).

(b) Tri-n-butylstannane (2.4420g) in benzene (10ml).

(c) Reaction mixtures:-

As in (ii).

(d) Reaction conditions:-

Temperature: 127°, time 24hr.

(e) Work-up procedure :-

As in (i).

(f) Gas chromatographic analysis:-

Column B (initial temperature 100° (5min.) then programmed to 120°). Calibration graphs obtained with mixtures of N-(3-butenyl)-N-methylaminobenzene (92d), 1,4-dimethyl-1,2,3,4-tetrahydroquinoline (93d) and N-methyl-2,3,4,5-tetrahydro-1-benzazepine (94d).

For table of results see following page.

(g) Results:-

Initial concn. of 89b (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92d** (%)	Relative yield of 93d (%)	Relative yield of 94d (%)	Absolute yield of reduction* (%)
0.073	-	-	-	-	-
0.073	-	-	-	-	-
0.073	0.074	36	64	0	50
0.073	0.074	36	64	0	59
0.073	0.148	38	62	0	95
0.073	0.149	37	63	0	91
0.073	0.299	43	57	0	85
0.073	0.300	43	57	0	87
0.073	0.600	48	52	0	89
0.073	0.599	48	52	0	85

* Where yields are less than 100% starting material (89b) was detected in the reaction mixtures.
** Unresolved doublet (see discussion).

(v) o-Vinyloxymethyleneiodobenzene (90)

(a) o-Vinyloxymethyleneiodobenzene (0.6925g) in benzene (10ml) and A.I.B.N. (6.5mg).

(b) Tri-n-butylstannane (2.5914g) in benzene (10ml).

(c) Reaction mixtures:-

As in (ii).

(d) Reaction conditions:-

Temperature: 127°, time 24 hr.

(e) Work-up procedure:-

As in (i).

(f) Gas chromatographic analysis:-

Column B (initial temperature 100° (5 min.) then programmed to 130°). Calibration graphs obtained with mixtures of internal standard, vinyloxymethylene-benzene (95), 1-methylphthalan (96) and isochroman (97).

For table of results see following page.

(g) Results:-

Initial concn. of 90 (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 95 (%)	Relative yield of 96 (%)	Relative yield of 97 (%)	Absolute yield of reduction* (%)
0.073	-	-	-	-	-
0.073	-	-	-	-	-
0.073	0.067	23	77	trace	37
0.073	0.093	28	72	trace	32
0.073	0.157	37	63	trace	86
0.073	0.152	35	65	trace	68
0.073	0.314	55	45	trace	99
0.073	0.318	55	45	trace	99
0.073	0.621	77	23	trace	99
0.073	0.603	74	26	trace	96

*Where yields are less than 100%, starting material (90) was detected in the reaction mixtures.

(vi) o-Allyloxymethyleneiodobenzene (91)

(a) o-Allyloxymethyleneiodobenzene (0.6809g) in benzene (10ml) and A.I.B.N. (2.3mg).

(b) Tri-n-butylstannane (6.2002g) in benzene (25ml).

(c) Reaction mixtures:-

As in (ii).

(d) Reaction conditions:-

Temperature: 128°, time 12 hr.

(e) Work-up procedure:-

As in (i).

(f) Gas chromatographic analysis:-

Column B (initial temperature 100° (5 min.) then programmed to 130°). Calibration graphs obtained with mixtures of internal standard, allyloxymethylene-benzene (98), 4-methylisochroman (99) and homo-isochroman (100).

For table of results see following page.

(g) Results:-

Initial concn. of 91 (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 98** (%)	Relative yield of 99 (%)	Relative yield of 100 (%)	Absolute yield of reduction* (%)
0.036	-	-	-	-	-
0.036	-	-	-	-	-
0.072	0.076	56	44	0	12
0.072	0.078	58	42	0	14
0.072	0.150	65	35	0	20
0.072	0.147	66	34	0	19
0.072	0.299	77	23	0	66
0.072	0.300	76	24	0	69
0.071	0.599	83	17	0	85
0.072	0.599	83	17	0	84

* Where yields are less than 100%, starting material (91) was detected in the reaction mixtures.
** Unresolved doublet (see discussion).

(vii) o-(3-Butenyl)iodobenzene (88c)

(a) o-(3-Butenyl)iodobenzene (0.6455g) in benzene (10ml) and A.I.B.N. (3.5mg).

(b) Tri-n-butylstannane (2.4255g) in benzene (10ml).

(c) Reaction mixtures:-

As in (ii).

(d) Reaction conditions:-

Temperature: 133°, time 24 hr.

(e) Work-up procedure:-

As in (i).

(f) Gas chromatographic analysis:-

Column A (temperature 110°). Calibration graphs obtained with mixtures of internal standard, (3-butenyl)benzene (92e), 1-methylindan (93e) and tetralin (94e).

For table of results see following page.

(g) Results:-

Initial concn. of 88c (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92e (%)	Relative yield of 93e (%)	Relative yield of 94e (%)	Absolute yield of reduction* (%)
0.078	-	-	-	-	-
0.073	0.067	9	91	trace	60
0.072	0.067	11	89	trace	66
0.073	0.137	19	81	trace	96
0.074	0.139	16	84	trace	99
0.073	0.287	37	63	trace	quant.
0.074	0.291	38	62	trace	quant.
0.073	0.570	50	50	trace	quant.
0.073	0.556	50	50	trace	quant.

* Where yields are less than 100%, starting material (88c) was detected in the reaction mixtures.

(viii) o-Vinyloxyiodobenzene (88d)

(a) o-Vinyloxyiodobenzene (0.0655g) in benzene (1.0ml) and A.I.B.N. (0.5mg).

(b) Tri-n-butylstannane (0.3770g) in benzene (1.0ml).

(c) Reaction mixtures:-

[0.5ml of (a), 0.2ml of (b) and benzene (0.6ml)] , and [0.5ml of (a) and 0.8ml of (b)] .

(d) Reaction conditions:-

Temperature 130°, time 21 hr.

(e) Work-up procedure:-

As in (i).

(f) Gas chromatographic analysis:-

Column A (temperature 120°). Calibration graphs obtained with mixtures of internal standard, vinyloxybenzene (92f) and 2,3-dihydrobenzofuran (94f).

For table of results see following page.

(g) Results:-

Initial concn. of 88d (moles/l)	Initial concn. of Bu_3SnH (moles/l)	Relative yield of 92f (%)	Relative yield of 94f (%)	Absolute yield of reduction (%)
0.092	0.166	100	0	92
0.100	0.830	100	0	94

PART IV

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